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(54) Title: SOLID-SUPPORTED INITIATORS AND FUNCTIONAL POLYMERS FOR USE IN ORGANIC SYNTHESIS AND COMBINATORIAL CHEMISTRY

(57) Abstract: Solid-supported initiator and functional polymers are described as well as methods for the preparation and use in solution phase, solid-phase organic synthesis, and combinational chemistry including use as initiators of solid-supported free-radical polymerization, as solid-supported scavengers for purification of crude solution phase reaction mixtures, as a stationary phase for solid-phase organic synthesis, and as solid-supported reagents in solution-phase organic synthesis.

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SOLID-SUPPORTED INITIATORS AND FUNCTIONAL POLYMERS FOR
USE IN ORGANIC SYNTHESIS AND COMBINATORIAL CHEMISTRY

FIELD OF THE INVENTION

5 The present invention relates to novel solid-supported initiators and solid-supported functional polymers, to processes for their preparation and to their use in organic synthesis and combinatorial chemistry.

BACKGROUND OF THE INVENTION

10 Organic synthesis has proven to be a highly effective means for preparation of molecules with useful biological activities which may be employed in the treatment of human, animal, and plant diseases. Combinatorial chemistry is a means of performing many organic syntheses concurrently or in parallel arrays, thereby increasing the rate at which compounds may be synthesized. In the preparation of
15 biologically active molecules via organic synthesis or combinatorial chemistry, a multi-step organic synthesis is usually required. Each step consists of reacting various chemicals to produce a product which is normally purified before continuing with the next step. Purification is typically the most time consuming part of organic synthesis. The time spent on purification is especially critical in combinatorial
20 chemistry since hundreds or even thousands of reactions are often carried out in parallel. Thus, methods which enable simple, rapid, and readily automated purification are of value to the practice of both organic synthesis and combinatorial chemistry.

 Solid-supported reagents which cause a chemical transformation of a
25 compound in solution provide a convenient and rapid means of purification since they can be removed from the desired product by filtration. Solid-supported reagents are typically prepared by chemical reactions that attach individual molecules of the desired reagent to a pre-formed solid support either by covalent bonding or ionic interaction.

30 Solid-supported scavenging reagents also provide a convenient and rapid means of purification since they selectively react with certain components of a mixture in solution, thereby removing them from solution to the solid phase where they can be easily separated from the unbound components by filtration. A solid-

supported scavenger may be used in one of two ways. First, it can be designed to selectively react with excess starting materials or other reactive impurities which contaminate the solution of a desired product. The resin and the sequestered contaminants are subsequently removed by filtration. Second, the scavenger resin
5 can also be designed to selectively react with the desired product. With the product sequestered on the resin, any contaminants may be rinsed away. The product is then chemically cleaved from the resin in a purified form. This latter use of a scavenging resin is often referred to as "catch and release." Solid-supported scavenging reagents are typically prepared by chemical reactions, which result in the covalent attachment
10 of individual molecules of the scavenger reagent to a pre-formed solid support.

Solid-phase synthesis provides yet another means of facile purification. In solid-phase synthesis, a solid support is covalently linked to the starting material of a synthesis. The reactions of the synthesis are carried out stepwise with excess reagents. After each reaction, the unreacted reagents and byproducts are rinsed from
15 the solid-supported product. At the end of the synthesis, the product is chemically cleaved from the solid-support in a substantially pure form. Solid phase synthesis resins are typically prepared by chemical reactions which result in the covalent attachment of linker functionalities to a pre-formed solid support. Alternatively, they may be prepared by aqueous suspension co-polymerization of unfunctionalized
20 monomers and monomers bearing the linker functionality. A suspension polymerization is typically carried out by vigorously stirring and heating one or more monomers and an initiator in water. The monomers and the initiator, being insoluble in water, form droplets. As they polymerize, the droplets form solid resin beads which are of sufficient molecular weight to be insoluble in organic solvents.
25 Aqueous suspension polymerization requires that any functionality on the monomers not be reactive with water nor promote dissolution of the monomer in water. This limits the range of monomers that may be utilized.

For a comprehensive review of the existing state of the art with respect to solid-supported reagents, solid-supported scavengers and solid phase organic
30 synthesis, see Obrecht D. and Villalgordo J.M., Tetrahedron Organic Chemistry Series, Volume 17, Solid-Supported Combinatorial and Parallel Synthesis of Small-Molecular-Weight Compound Libraries.

A disadvantage with some solid-supported reagents and solid-supported scavengers is their low loading of reactive groups per gram of solid support. For

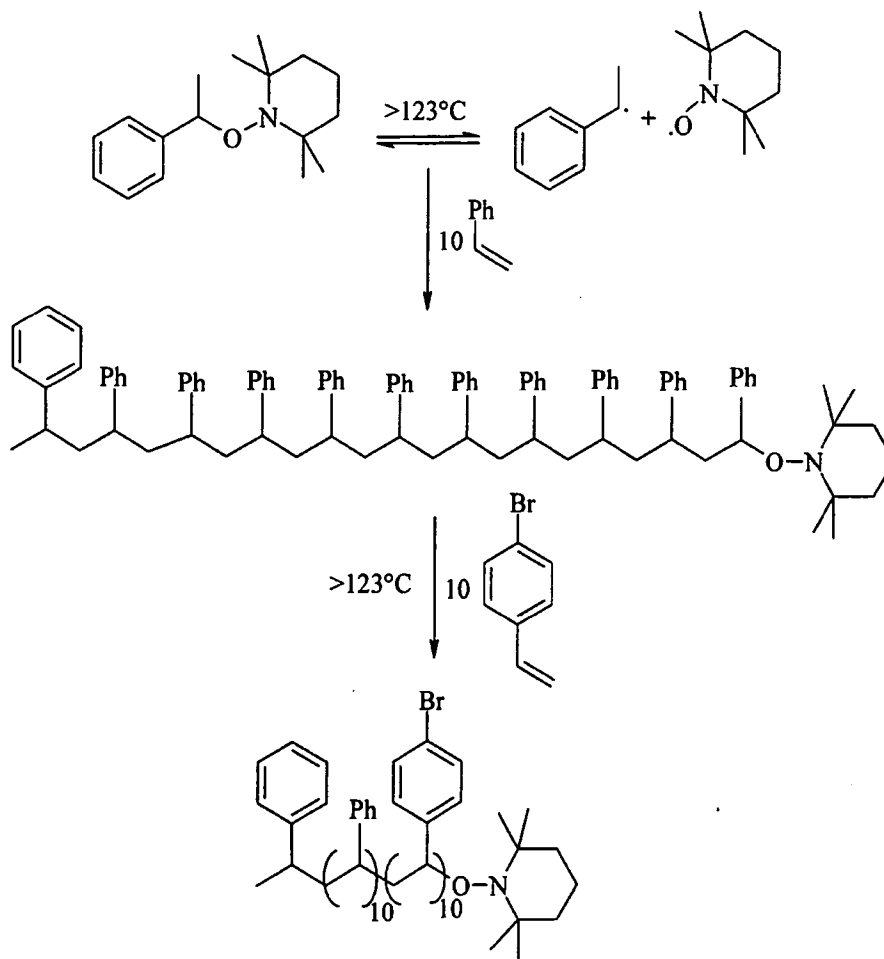
instance, an isocyanate scavenger resin with 1.1 mMol of isocyanate groups per gram of resin has recently been described (Booth R.J. and Hodges J.C., Polymer-Supported Quenching Reagents for Parallel Purification, *J. Am. Chem. Soc.*, 1997;119:4882-4886). An isocyanate resin with double or triple this loading would
5 be very useful, since less scavenger resin would need to be added in order to affect the same degree of purification. It is impossible to attach such a high loading of isocyanate groups to the resin by the method of this paper because of a competing reaction that results in the formation of urea crosslinks on the resin instead of isocyanate functionality.

10 A difficulty that is frequently encountered in solid-phase synthesis is the unpredictable reaction kinetics when the starting material of a reaction is attached to a solid support. The source of this difficulty is related to steric crowding around some but not all of the starting material molecules that is caused by the resin. In other words, some of the starting material molecules are attached deep in pores of
15 the resin and have low accessibility to reagents in solution. These hidden molecules react slowly compared to molecules that are attached at the surface. Typically a three- to ten-fold excess of reactants is used in the solution that bathes the solid-supported substrate in order to overcome the sluggish reactivity of hidden starting material molecules and drive the reaction to completion. A resin wherein all of the
20 starting material molecules had greater and more equal exposure to reagents would more closely resemble a solution phase reaction and thus would both be more kinetically predictable and require a smaller excess of reactants.

The synthesis of block co-polymers by living free-radical polymerization has been described in the literature. For a recent and comprehensive review on living
25 free-radical polymerization see Malmstroem Eva E.; Hawker Craig J., Macromolecular engineering via "living" free-radical polymerizations, *Macromol. Chem. Phys.*, 1998;199:923-935. One class of living free-radical polymerization reactions makes use of nitroxide reagents to initiate the reaction and cap the growing polymer chain. For example, 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO),
30 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl (OH-TEMPO), 4-oxo-2,2,6,6-tetramethylpiperidine-1-oxyl (oxo-TEMPO) and related O-alkyl derivatives such as 1-Phenyl-1-(2',2',6',6'-tetramethyl-1'-piperidinyloxy)-ethane (1-Phenylethyl-TEMPO), are useful nitroxide reagents in living free-radical polymerization. A variety of useful nitroxide reagents are described by

Chang Hun Han, Marco Drache, and Gudrun Schmidt-Naake in *Die Angewandte Makromolekulare Chemie*, 1999;264:73–81. A variety of useful alkoxyamines and their performance in living free radical polymerization reactions are described by Didier Benoit, Vladimir Chaplinski, Rebecca Brnslau and Craig J. Hawker in *The Journal of the American Chemical Society*, 1999; 121:3904–20. The use of 1-Phenylethyl-TEMPO in a living free-radical polymerization is described in Scheme 1 below.

Scheme 1



Heating 1-Phenylethyl-TEMPO above 123°C causes it to reversibly fragment into a TEMPO radical and a phenylethyl radical. If this is done in the presence of an excess of styrene, the phenylethyl radical initiates polymerization of the styrene. The resulting polystyrene has a low degree of polydispersity. In other words, the polymer chain length is highly homogeneous and related to the stoichiometry of the starting

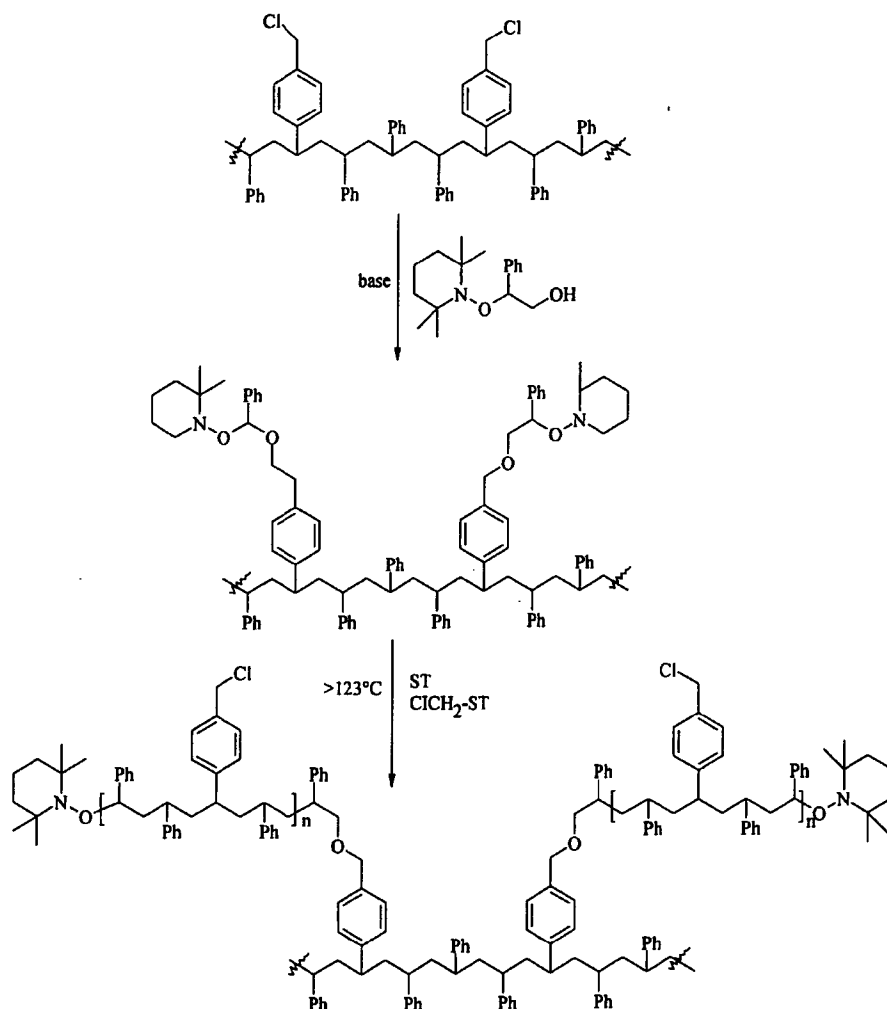
reaction mixture. Each molecule of 1-Phenylethyl-TEMPO grows one polymer chain of approximately 10 monomer units, the terminus of which is capped with a TEMPO residue. Subsequently, it is possible to use the first polymer as an initiator for an even larger polymer as shown by the second vertical arrow of Scheme 1.

5 Heating of the first polymer with excess 4-bromostyrene causes continued polymerization to give a polymer of approximately twice the number of monomer units in two blocks, one of which is polystyrene and the other of which is poly(4-bromostyrene). The term "living free-radical polymerization" arises from the potential ability to start, stop, and continue polymerization reactions in repeated
10 cycles. The polymerization reaction "lives" a long time since chain termination reactions that would "kill" the polymerization reaction are inhibited by the presence of the TEMPO radical.

Scheme 2 shows an alternate method by which nitroxide initiators may be used to create block co-polymers. Soluble poly(styrene-chloromethylstyrene) is
15 reacted with 2-hydroxy-1-phenylethyl-TEMPO in the presence of a strong base. This results in a nitroxide functionalized polymer wherein an ether linkage connects 1-Phenethyl-TEMPO to the soluble polystyrene. This nitroxide functionalized polymer is heated with a mixture of styrene and chloromethylstyrene to form a branched polymer product wherein chains of poly(styrene-chloromethylstyrene)
20 emanate from the phenyl groups of the core polystyrene.

-6-

Scheme 2



The polymerization of styrene and methyl methacrylate onto silicon wafers is described by M. Husseman, et al. in *Macromolecules*, 1999;32:1424–1431. The resulting polymer brushes attached to silicon wafers have applications in microelectronics.

US Patent 5,767,238 titled "Inverse Solid Phase Synthesis" discloses: "A method of inverse solid phase synthesis comprising the steps of: (a) reacting at least two reactants in a solution to obtain a product; and (b) removing at least one unreacted said reactants with a solid phase matrix wherein said solid phase matrix covalently binds said at least one unreacted said reactants, leaving substantially all of

said product in said solution.” This patent is pertinent to the concept of solid-supported scavenging that is described above.

Preparation of other functional polymers have been described in the literature. An extensive review of functional polymer preparations has recently been
 5 edited by A.O. Patil, D.N. Schulz, and B.M. Novac (*Functional Monomers, Modern Synthetic Methods and Novel Structures*, ACS Symposium Series 704, The American Chemical Society, 1997, 347 pages).

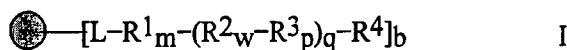
The aforementioned references do not describe or suggest the novel solid-supported, functional polymers disclosed herein, nor do they teach their use in
 10 organic synthesis and combinatorial chemistry, nor do they teach the processes for their preparation that are described in the present invention.

Thus, we have surprisingly and unexpectedly found that insoluble solid supports may be chemically modified to contain multiple cyclic nitroxide sites which can act as initiators to radical polymerization. Furthermore, solid-supported
 15 functional polymers may be prepared from these solid-supported initiators. Particularly novel is the ability to polymerize monomers with water-sensitive functional groups onto pre-formed bead-shaped supports which overcomes a limitation of aqueous suspension polymerization methods. The macromolecular structure of these solid-supported functional polymers allows properties such as
 20 greater solvent accessibility to reaction sites and higher loading levels of reagent functionality compared to known solid-supported reagents, solid-supported scavengers, and supports for solid phase synthesis. These properties dramatically enhance the utility of compounds of the present invention in organic synthesis and combinatorial chemistry.

25


SUMMARY OF THE INVENTION :

Accordingly, a first aspect of the present invention is a compound of Formula I,



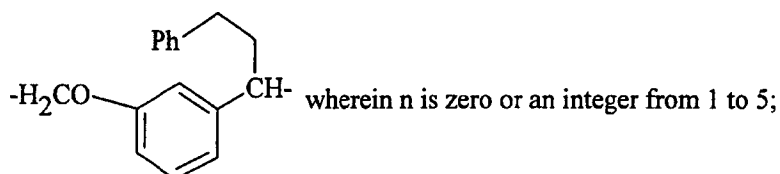
wherein

30

 is an insoluble solid support selected from the group consisting of:
 poly(styrene-divinylbenzene), macroreticular poly(styrene-divinylbenzene),

polystyrene which is radiation grafted to polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene), and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) wherein the insoluble solid support is in a shape selected from a bead, a tube, a rod, a ring, a disk, or a well;

L is $-\text{CH}_2-$, $-\text{C}(\text{CH}_3)_2-$, $-\text{CH}(\text{CH}_3)-$, $-(\text{CH}_2)_n\text{CH}(\text{CN})-$, $-(\text{CH}_2)_n\text{CH}(\text{CO}_2\text{Me})-$, $-(\text{CH}_2)_n\text{CH}(\text{Ph})-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3, \text{Ph})-$, $-\text{CH}(\text{CH}_2\text{CH}_2\text{Ph})-$, or



m is zero or an integer from 1 to 100;

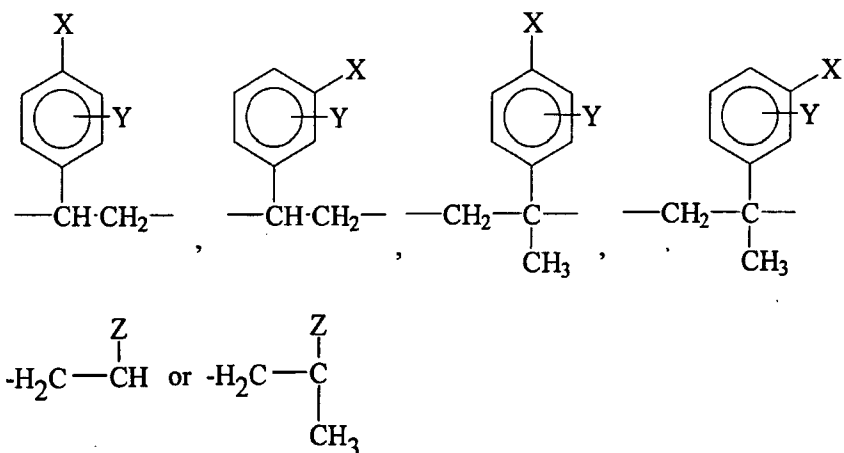
w is an integer from 1 to 10;

p is zero or an integer from 1 to 10;

q is zero or an integer from 1 to 300;

b is mMol content of initiator or solid-supported polymer per gram of insoluble solid support and is about 0.1 to about 5.0 mMol per gram;

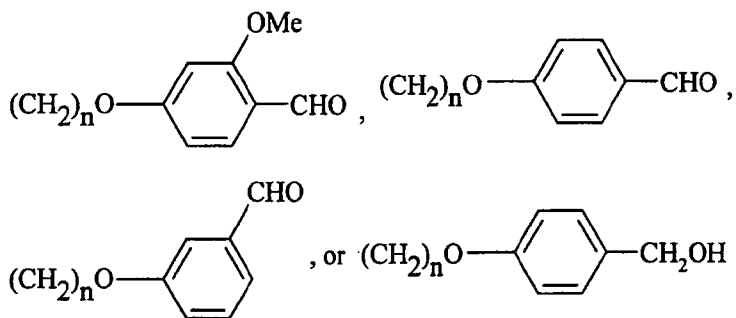
R^1 , R^2 , and R^3 are each independently the same or different and are



wherein

X is H, F, $(\text{CH}_2)_n\text{Cl}$, $(\text{CH}_2)_n\text{Br}$, $(\text{CH}_2)_n\text{I}$, $\text{B}(\text{OH})_2$, $(\text{CH}_2)_n\text{CH}=\text{CH}_2$, NCO , CH_2NCO , $\text{CH}(\text{CH}_3)\text{NCO}$, $\text{C}(\text{CH}_3)_2\text{NCO}$, CO_2Me , CO_2Et , $\text{CO}_2(t\text{-Bu})$, CO_2H , COCl , $\text{CO}_2\text{CH}(\text{CF}_3)_2$, CO_2Ph , $\text{CO}_2(\text{pentafluorophenyl})$,

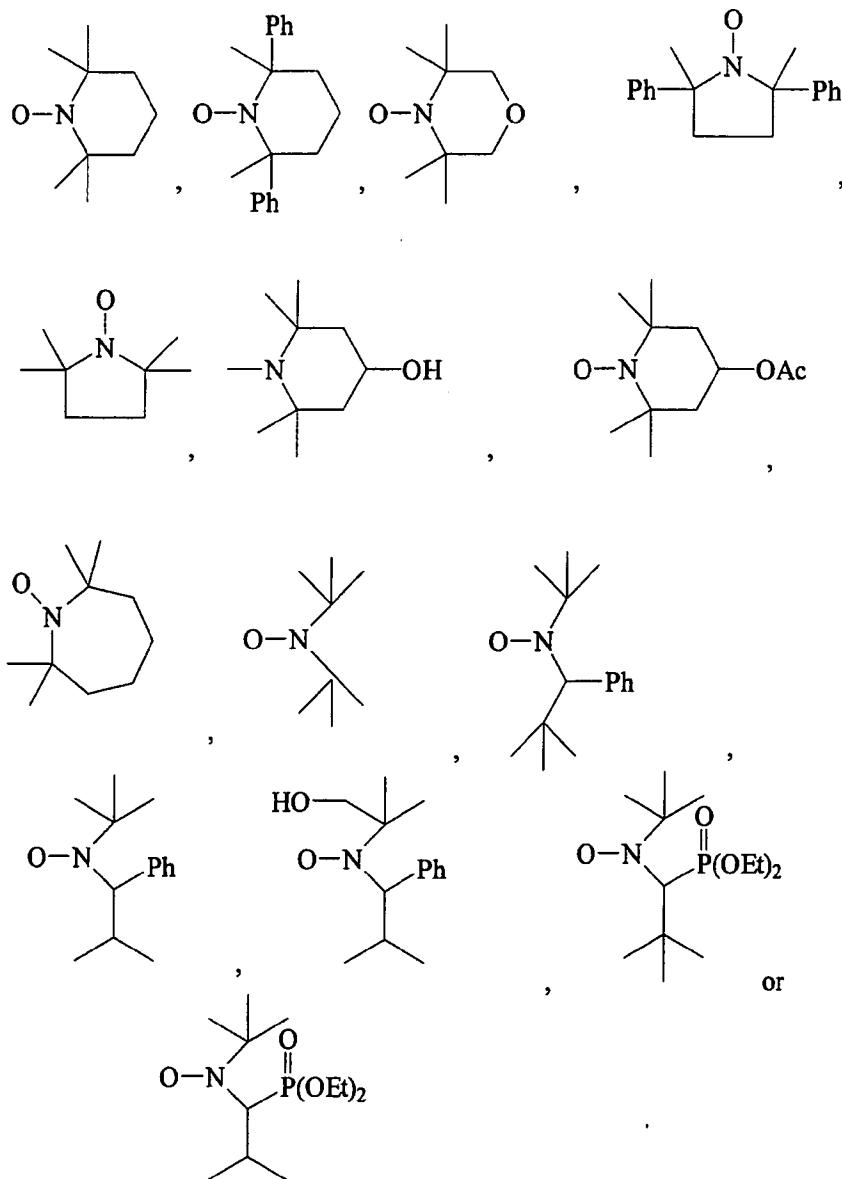
$\text{CO}_2(\text{pentachlorophenyl})$, $\text{CO}_2(\text{N-succinimidyl})$, $\text{C}(\text{OMe})_3$, $\text{C}(\text{OEt})_3$,
 $(\text{CH}_2)_n\text{OH}$, $(\text{CH}_2)_n\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $(\text{CH}_2)_n\text{SH}$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{SH}$,
 $\text{CH}_2)_n\text{NHC}(=\text{S})\text{NH}_2$, $(\text{CH}_2)_n\text{NH}_2$, $(\text{CH}_2)_n\text{N}(\text{Me})_2$, $(\text{CH}_2)_n\text{N}(\text{Et})_2$,
 $(\text{CH}_2)_n(\text{iPr})_2$, $\text{CH}(\text{CH}_3)\text{NH}_2$, $\text{C}(\text{CH}_3)_2\text{NH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$,
 5 $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$,
 $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$,
 $(\text{CH}_2)_n(\text{morpholin-4-yl})$, $(\text{CH}_2)_n(\text{piperidin-1-yl})$,
 $(\text{CH}_2)_n(4\text{-methypiperazin-1-yl})$, $\text{N}(\text{SO}_2\text{CF}_3)_2$, $(\text{CH}_2)_n\text{CHO}$,
 $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{iPr})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{tBu})_2\text{H}$,
 10 $(\text{CH}_2)_n\text{Si}(\text{Ph})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Ph})(\text{tBu})\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{Cl}$,
 $(\text{CH}_2)_n\text{Si}(\text{i-Pr})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{tBu})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Ph})_2\text{Cl}$,
 $(\text{CH}_2)_n\text{Si}(\text{tBu})(\text{Ph})\text{Cl}$, $\text{P}(\text{Ph})_2$, $\text{P}(o\text{-tolyl})_2$,



15 wherein n is zero or an integer from 1 to 5;

Y is H, Cl, Br, F, OH, or OMe;

Z is s NCO, CO_2Me , CO_2Et , $\text{CO}_2(\text{i-Pr})$, $\text{CO}_2(n\text{-Bu})$, $\text{CO}_2(\text{t-Bu})$, CN, CO_2H ,
 COCl , $\text{CO}_2\text{CH}(\text{CF}_3)_2$, $\text{CO}_2(\text{pentafluorophenyl})$, $\text{CO}_2(\text{pentachlorophenyl})$,
 CO_2Ph , $\text{CO}_2(\text{N-succinimidyl})$, $\text{C}(\text{OMe})_3$, $\text{C}(\text{OEt})_3$, $\text{CON}(\text{OCH}_3)\text{CH}_3$,
 20 CHO , CH_2OH , or $\text{C}(\text{CH}_3)_2\text{OH}$; and

R⁴ is

A second aspect of the present invention is a process for preparing a
 5 compound of Formula I, as described above, which comprises conversion of a solid
 support to a compound of Formula I in one to eight synthetic steps, rinsing
 thoroughly with one or more solvents after each synthetic step.

A third aspect of the present invention is the use a compound of Formula I,
 as described above, in solution phase organic synthesis, solid-phase organic

synthesis, and combinatorial chemistry, including its use as an initiator of solid-supported free-radical polymerization, its use as a solid-supported scavenger for purification of crude solution phase reaction mixtures, its use as a stationary phase for solid-phase organic synthesis, and its use as solid-supported reagents in solution phase organic synthesis.

DETAILED DESCRIPTION OF THE INVENTION

The following Table 1 provides a list of definitions and abbreviations used in the present invention.

Table 1. Definitions and Abbreviations

<u>Term</u>	<u>Definition</u>
Byproduct	An undesirable product of a reaction which comprises at least two mole percent of the crude product. Isomers, enantiomers and diastereomers of the desired product are not considered to be byproducts within the scope of this invention.
Crude reaction product	The result of a chemical reaction before any purification. This term is synonymous with crude product and crude reaction mixture.
Enhancing purity	A) For a single desired compound: The process of removing excess or unreacted starting reagents to the limit of detection by TLC or by NMR spectroscopy and/or reducing the content of any single byproduct to less than two mole percent, exclusive of solvents. B) For a combinatorial mixture of desired compounds: The process of removing excess or unreacted starting reagents and or reducing the content of a byproduct using a procedure that has been validated on crude reaction products of analogous single compounds.
Solid support	A material which does not dissolve in organic and/or aqueous solvents and mixtures thereof.
Insoluble polymer	A polymeric compound which by virtue of its structure and high molecular weight is incapable of dissolving in organic and/or aqueous solvents and mixtures thereof.

Solid-supported scavenger A molecule which is attached to a an insoluble solid and binds to a starting reagent and/or to a byproduct in a covalent and/or ionic manner, thereby removing it from a solution. A synonym for a polymer-supported quench reagent.

Table 1. Definitions and Abbreviations (cont'd)

<u>Term</u>	<u>Definition</u>
Resin	A synonym for an insoluble polymer, usually in beaded form.
Resin swelling solvent	A solvent which penetrates pores of an insoluble polymer and causes it to increase in volume.
Soluble polymer	A polymeric compound which by virtue of its structure and molecular weight is able to dissolve in selected solvents.
Radiation grafting	The process for preparing a complex polymeric compound which entails treating a mixture of base polymer such as, for example, polyethylene, polypropylene, poly(ethylene-tetrafluoroethylene) or poly(tetrafluoroethylene), and a monomer such as, for example, styrene with ionizing radiation. This process results in the polymerization of polystyrene onto the base polymer.
Grafted copolymer	A complex polymer that is produced by radiation grafting. A synonym for a radiation grafted copolymer.
Solid-supported polymer	A polymeric compound which is covalently attached to an insoluble solid.
Functional polymer	A polymer which bears multiple instances of chemically reactive functional groups.
Macroreticular	A property of insoluble polymers indicating a rigid, highly crosslinked polymer which does not swell in any solvent and is porous.
Polydispersity	A polymer property indicating variable length and molecular weight.
Monodispersity	A polymer property indicating highly uniform length and molecular weight
IR	Infrared spectroscopy
MS	Mass spectrometry
^1H -NMR	Proton nuclear magnetic resonance spectroscopy

<u>Table 1. Definitions and</u>	<u>Abbreviations (cont'd)</u>
<u>Abbreviation</u>	<u>Structural Group</u>
Ph	Phenyl
Me	Methyl or $-\text{CH}_3$
Et	Ethyl or $-\text{CH}_2\text{CH}_3$
iPr	Isopropyl or $-\text{CH}(\text{CH}_3)_2$
Bu	Butyl or $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$
<i>t</i> -Bu	<i>Tertiary</i> -Butyl or $\text{C}(\text{CH}_3)_3$
NCO	Isocyanate
BA	Butyl acrylate
BMA	Butyl methacrylate
ST	Styrene or vinylbenzene
MeST	α -Methylstyrene or 2-phenylpropene
DVB	1,2-Divinylbenzene
Br-ST	4-Bromostyrene
3-Br-ST	3-Bromostyrene
HO-ST	4-Hydroxystyrene
3-HO-ST	3-Hydroxystyrene
$\text{HOCH}_2\text{-ST}$	Hydroxymethyl-styrene (typically obtained as a mixture of 3- and 4-vinyl-benzyl alcohol)
$\text{ClCH}_2\text{-ST}$	Chloromethyl-styrene (typically obtained as a mixture of 3- and 4-vinyl-benzyl chloride)
H-DIPS-ST	(4-vinyl)phenyl-diisopropyl-silane
Cl-DIPS-ST	(4-vinyl)phenyl-diisopropyl-chlorosilane
$\text{F}_5\text{-ST}$	2,3,4,5,6-pentafluorostyrene
TMI	3-(2-Propenyl)- α,α -dimethylbenzyl isocyanate
DCM	Dichloromethane
MeOH	Methanol
DMF	N,N-Dimethylformamide
THF	Tetrahydrofuran
EtOAc	Ethyl acetate
EtOH	Ethanol
MeCN	Acetonitrile

<u>Table 1. Definitions and</u>	<u>Abbreviations (cont'd)</u>
TEMPO	2,2,6,6-Tetramethylpiperidinyloxy free radical
TEMPO-H	1-Hydroxy-2,2,6,6-tetramethylpiperidine

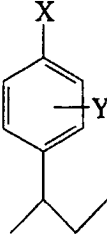
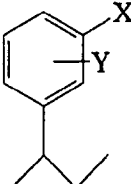

PhNCO	Phenyl isocyanate
BuNCO	Butyl isocyanate
TFA	Trifluoroacetic acid
TFA-d	Deuterated trifluoroacetic acid
OsO ₄	Osmium tetroxide
NMO	N-Methylmorpholine-N-oxide
Ph ₃ P	Triphenylphosphine
9BBU	9-Borabicyclo[3.3.1]nonane
DEAD	Diethyl azodicarboxylate
KBr	Potassium bromide
	An attached phenyl ring bearing substituents X and Y wherein X is fixed at the para position and Y may occupy any or all of the remaining ortho and meta positions. A position not occupied by X or Y is occupied.
	An attached phenyl ring bearing substituents X and Y wherein X is fixed at the meta position and Y may occupy any or all of the remaining ortho, para or meta positions. Any position not occupied by X or Y is occupied by a hydrogen atom (H).


Table 1. Definitions and Abbreviations (cont'd)

Abbreviation	Solvents and Reagents
	An insoluble solid support selected from the group consisting of: poly(styrene-divinylbenzene), macroreticular poly(styrene-divinylbenzene), polystyrene which is radiation grafted to polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene), and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) wherein the insoluble solid support is in a shape selected from a bead, a tube, a rod, a ring, a disk, or a well

In the first aspect of the present invention, a preferred compound of

Formula I is one, wherein is an insoluble solid support selected from the group

consisting of: poly(styrene-divinylbenzene) and macroreticular poly(styrene-divinylbenzene) in the shape of a bead.

In the first aspect of the present invention, a more preferred compound of Formula I is one wherein  is an insoluble solid support selected from the group consisting of: polystyrene which is radiation grafted to polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene) and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) in the shape selected from a tube, a rod, a ring, a disk, or a well.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein L is $-\text{CH}_2-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3, \text{Ph})-$, or $-\text{CH}(\text{CH}_2\text{CH}_2\text{Ph})-$.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein m and q are equal to zero.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein m is equal to zero, and q is an integer from 1 to 300.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein m is an integer from 1 to 100, and q is an integer from 1 to 300.

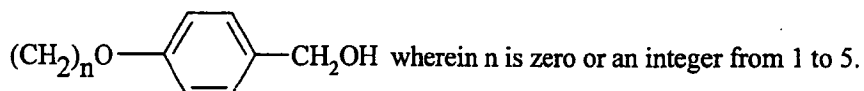
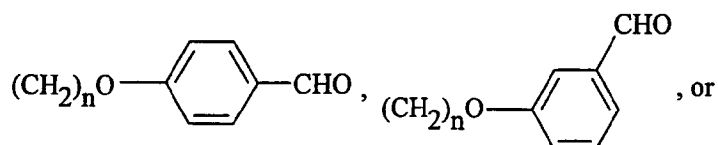
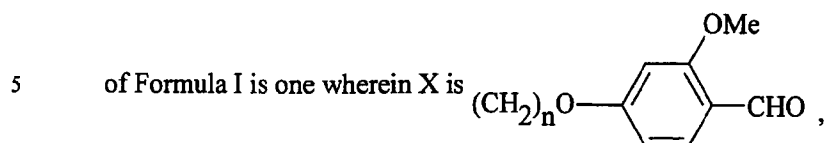
In the first aspect of the present invention, another more preferred compound of Formula I is one wherein X is NCO, CH_2NCO , $\text{CH}(\text{CH}_3)\text{NCO}$ or $\text{C}(\text{CH}_3)_2\text{NCO}$, and Y is H.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein X is $(\text{CH}_2)_n\text{NH}_2$, $(\text{CH}_2)_n\text{N}(\text{Me})_2$, $(\text{CH}_2)_n\text{N}(\text{Et})_2$, $(\text{CH}_2)_n(\text{iPr})_2$, $\text{CH}(\text{CH}_3)\text{NH}_2$, $\text{C}(\text{CH}_3)_2\text{NH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $(\text{CH}_2)_n(\text{morpholin-4-yl})$, $(\text{CH}_2)_n(\text{piperidin-1-yl})$, or $(\text{CH}_2)_n(4\text{-methypiperazin-1-yl})$ wherein n is zero or an integer from 1 to 5.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein X is $(\text{CH}_2)_n\text{SH}$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{SH}$, or $\text{CH}_2)_n\text{NHC}(=\text{S})\text{NH}_2$ wherein n is zero or an integer from 1 to 5.

In the first aspect of the present invention, another more preferred compound of Formula I is one wherein X is $(\text{CH}_2)_n\text{Cl}$, $(\text{CH}_2)_n\text{Br}$, $(\text{CH}_2)_n\text{I}$, $(\text{CH}_2)_n\text{OH}$, or $(\text{CH}_2)_n\text{CH}(\text{OH})\text{CH}_2\text{OH}$ wherein n is zero or an integer from 1 to 5.

In the first aspect of the present invention, another more preferred compound



In the first aspect of the present invention, another more preferred compound of Formula I is one wherein X is CO_2Me , CO_2Et , $\text{CO}_2(t\text{-Bu})$, CO_2H , COCl ,
10 $\text{CO}_2\text{CH}(\text{CF}_3)_2$, CO_2Ph , $\text{CO}_2(\text{pentafluorophenyl})$, $\text{CO}_2(\text{pentachlorophenyl})$,
 $\text{CO}_2(\text{N-succinimidyl})$, $\text{C}(\text{OMe})_3$, or $\text{C}(\text{OEt})_3$.

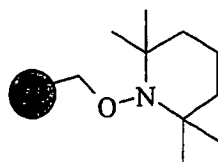
In the first aspect of the present invention, a most preferred compound of Formula I is one wherein Z is NCO , CO_2Me , CO_2Et , $\text{CO}_2(i\text{-Pr})$, $\text{CO}_2(n\text{-Bu})$,
 $\text{CO}_2(t\text{-Bu})$, CN , CO_2H , COCl , $\text{CO}_2\text{CH}(\text{CF}_3)_2$, $\text{CO}_2(\text{pentafluorophenyl})$,
15 $\text{CO}_2(\text{pentachlorophenyl})$, CO_2Ph , $\text{CO}_2(\text{N-succinimidyl})$, $\text{C}(\text{OMe})_3$, $\text{C}(\text{OEt})_3$,
 $\text{CON}(\text{OCH}_3)\text{CH}_3$, CHO , CH_2OH , or $\text{C}(\text{CH}_3)_2\text{OH}$.


In the first aspect of the present invention, another most preferred compound of Formula I is one wherein X is $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{H}$,
 $(\text{CH}_2)_n\text{Si}(i\text{Pr})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{Cl}$ or $(\text{CH}_2)_n\text{Si}(i\text{Pr})_2\text{Cl}$.

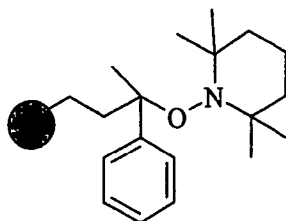
20 In the first aspect of the present invention, another most preferred compound of Formula I is one wherein R^4 is CH_2 and R^5 is CH_3 .


Particularly valuable in the first aspect of the present invention is a compound selected from the group consisting of:

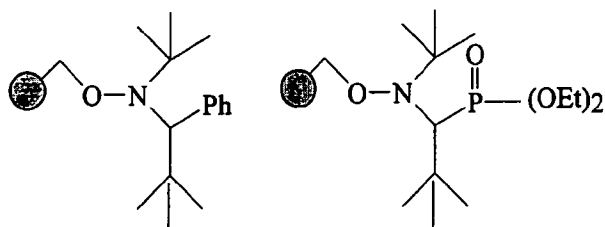
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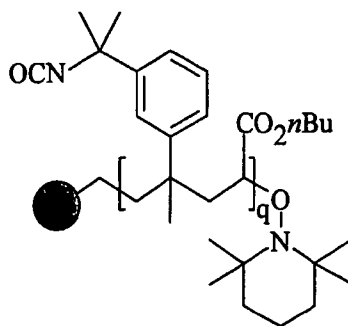
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, and the nitrogen content is 0.1 to 4 mMol per gram;




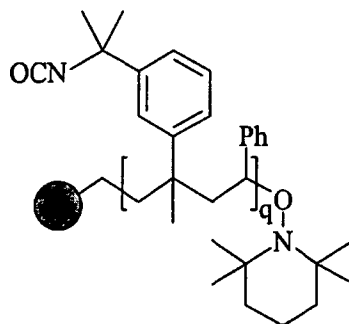
5 wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, and the nitrogen content is 0.1 to 4 mMol per gram;




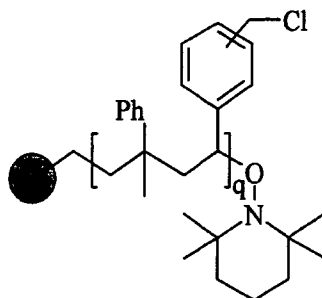
10 wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, and the nitrogen content is 0.1 to 4 mMol per gram;




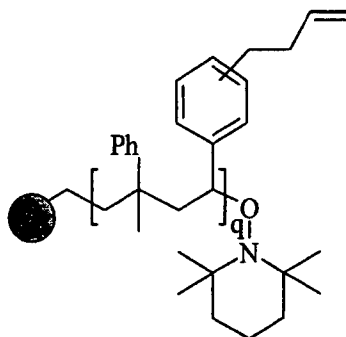
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30 and the isocyanate content is 1 to 4 mMol per gram;



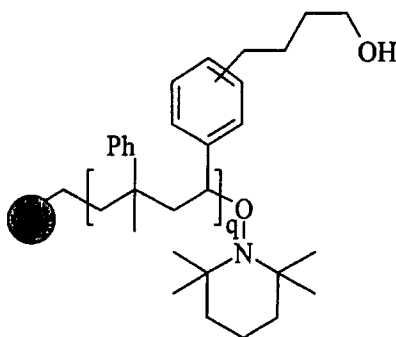
5 wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30 and the isocyanate content is 1 to 4 mMol per gram;



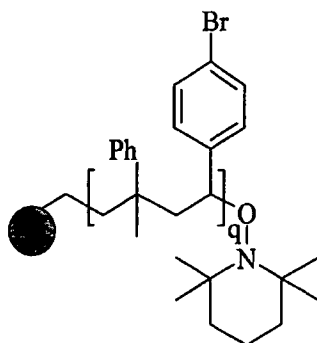
10 wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the chlorine content is 1 to 4 mMol per gram;



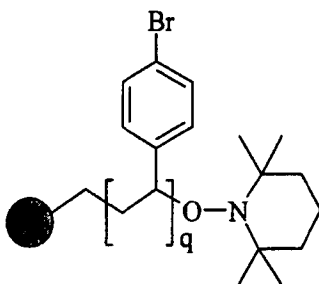
wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the alkene content is 1 to 4 mMol per gram;




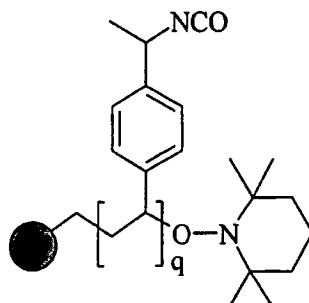
5 wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the hydroxyl content is 1 to 4 mMol per gram;




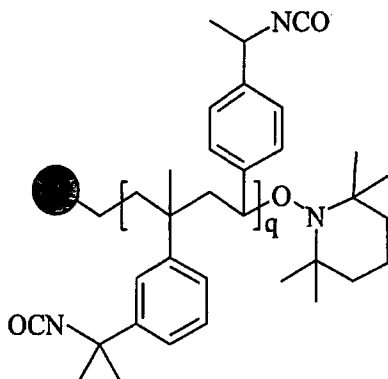
10 wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the bromine content is 1 to 4 mMol per gram;




wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 80 with an average of between 10 and 60, and the bromine content is 1 to 6 mMol per gram;

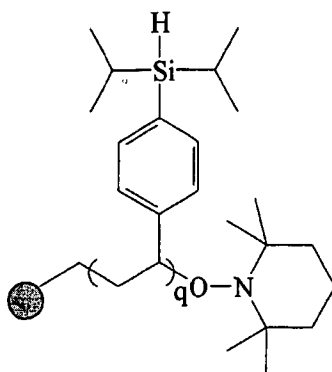



5 wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 80 with an average of between 10 and 60, and the isocyanate content is 1 to 6 mMol per gram; and




10 wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the isocyanate content is 1 to 6 mMol per gram.

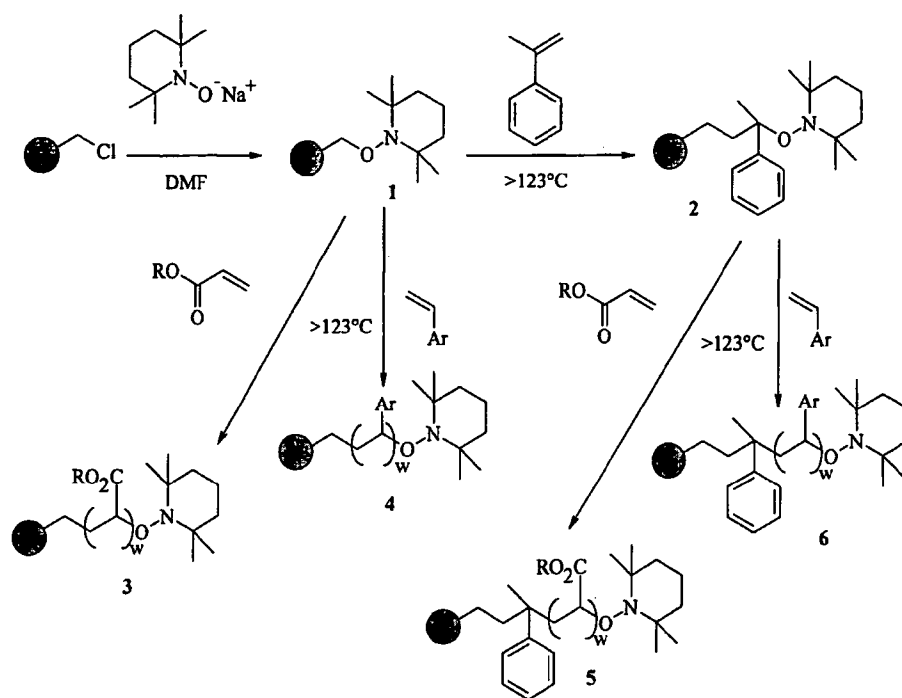
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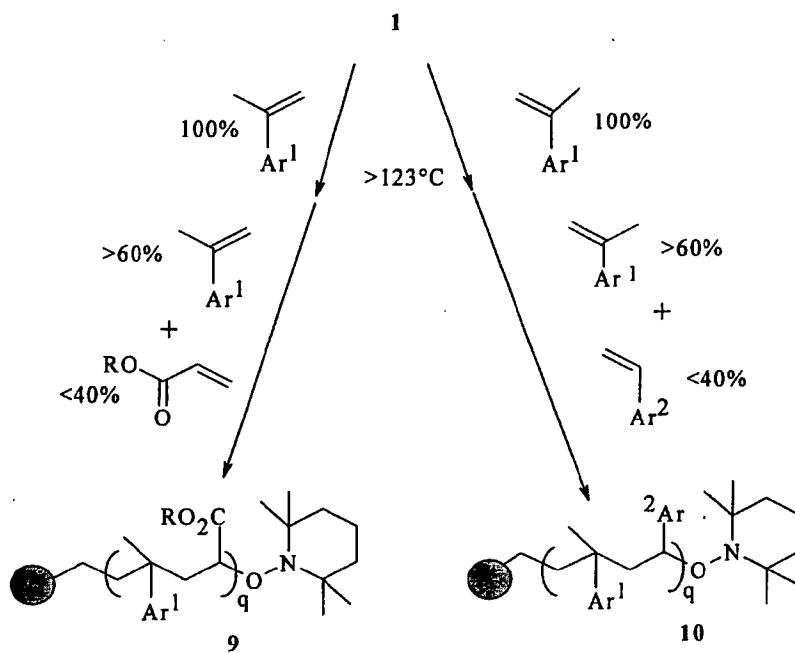
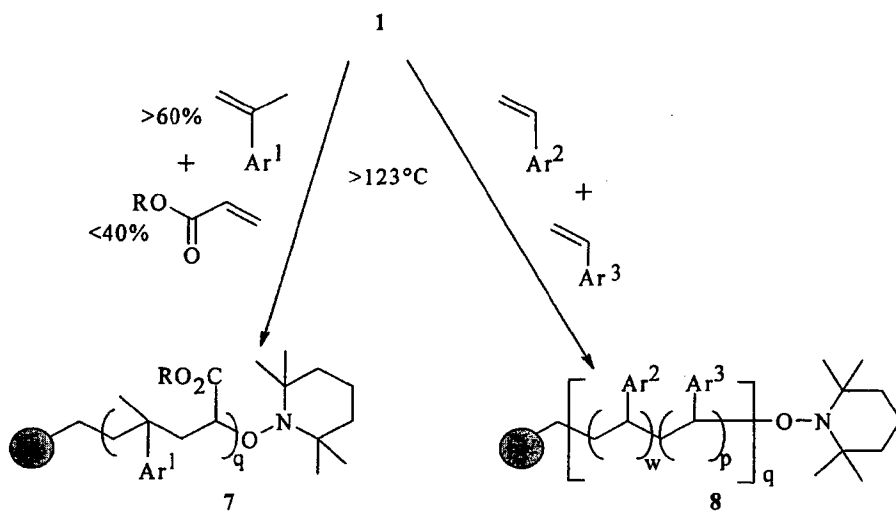
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 100 with an average between 10 and 60, and the Si content is 1 to 6 mMol per gram.

- 5 A compound of Formula I wherein , L, R¹, m, R², w, R³, p, q, R⁴, R⁵, and b are as defined above can be prepared by the general procedures, as set forth in Schemes 3-6. These schemes provide typical procedures for preparing compounds of Formula I. All structures in Schemes 3-6 which are numbered by bold arabic numerals represent a compound of Formula I.

Scheme 3

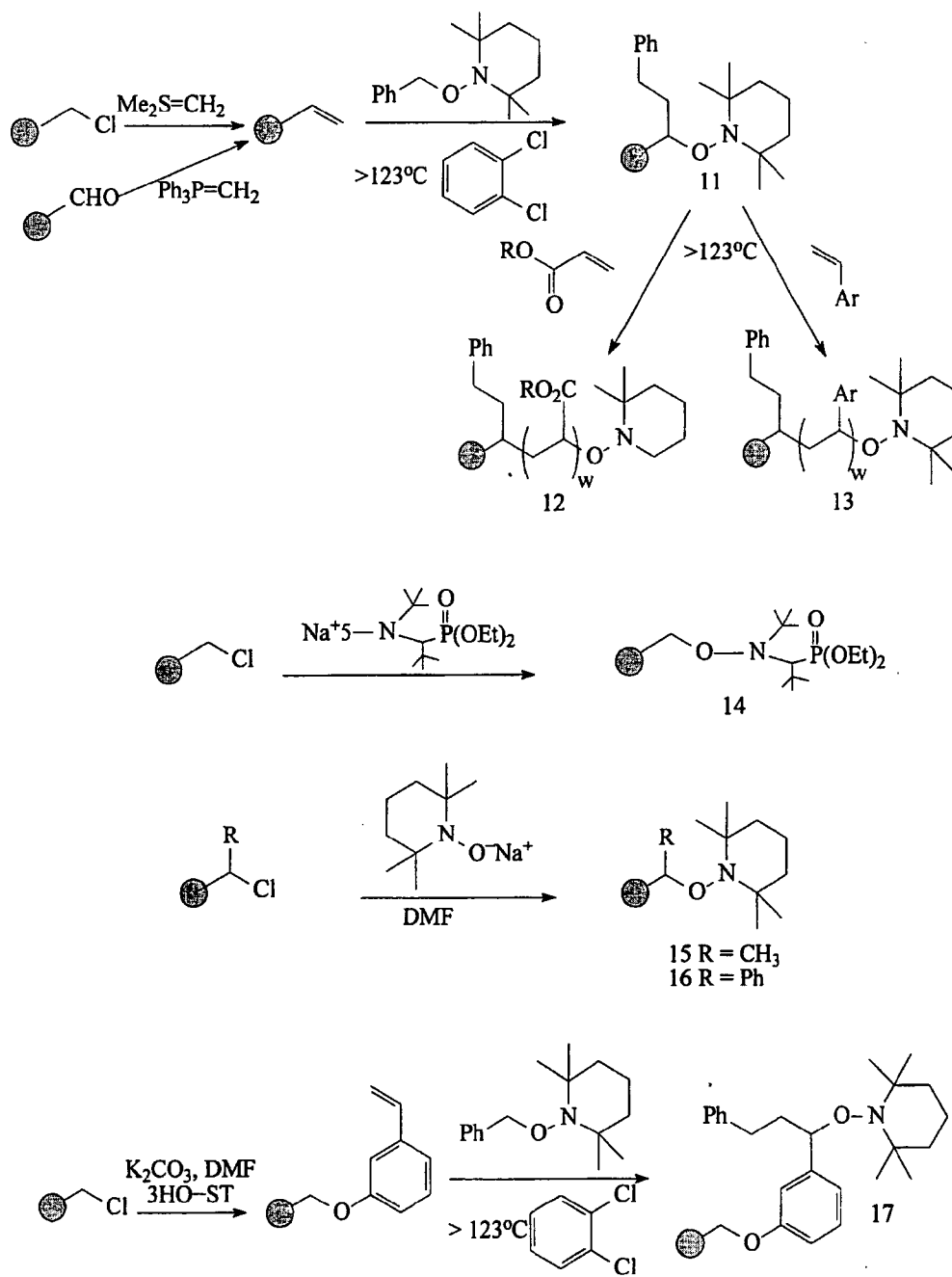


Scheme 4



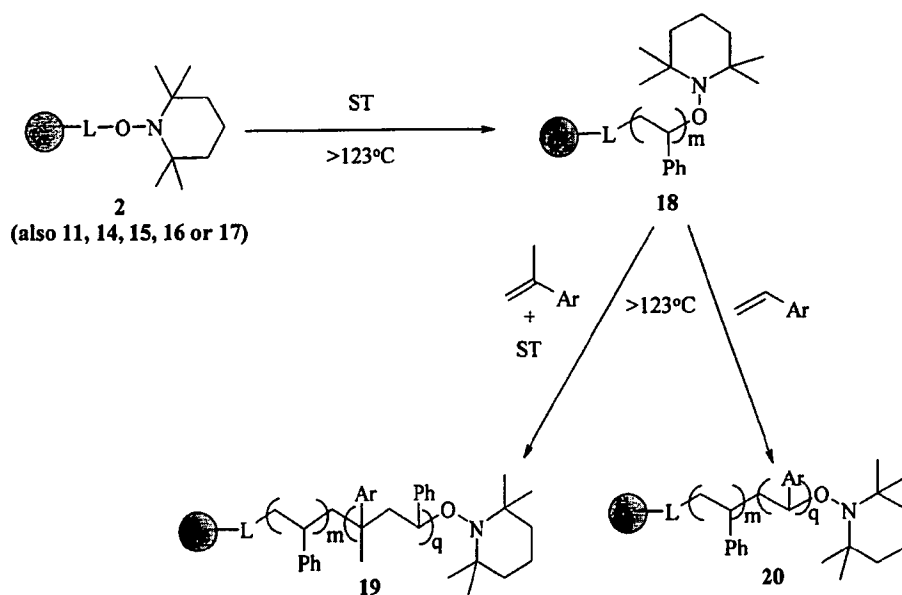
-24-

Scheme 5



-25-

Scheme 6



A process for the preparation of a compound of Formula I may be one or two chemical transformations from known or commercially available solid supports. For example, the chemical modification of an insoluble support to covalently attach multiple cyclic nitroxide substituents to the solid support gives a compound of Formula I wherein m and q are zero. Scheme 3 shows two representative illustrations. Reaction of the sodium salt of TEMPO with Merrifield resin in DMF gives 1. Heating of 1 in the presence of MeST gives 2. Both 1 and 2 are useful as solid-supported initiators of free radical polymerization. Scheme 5 shows the preparation of 11, 14, 15, 16, and 17 which are useful as solid-supported initiators of free radical polymerization.

Additional processes for preparing a compound of Formula 1 are shown in Schemes 3, 4, and 10. This process comprises: (1) chemical modification of an insoluble support to covalently attach multiple cyclic nitroxide substituents to the solid support, (2) heating the nitroxide-modified solid support with one or more substituted styrene and/or acrylate monomers to grow polymeric chains onto the solid support, (3) rinsing of the solid-supported polymer to remove excess monomer(s) and unattached polymer(s), and (4) chemical transformation of functional groups on the polymer as necessary to create a compound of Formula 1 wherein m is zero and q is an integer from 1 to 300.

Heating the solid-supported initiator, 1 with an acrylate monomer affords the solid-supported polymer 3 and heating 1 with a styrene monomer affords 4 (Scheme 3). When the point of attachment of the cyclic nitroxide in the solid-supported initiator is a primary carbon, as is the case for 1, the polymerization reaction results in solid-supported polymers which have a high degree polydispersity. That is to say that individual polymer chains of 3 and 4 vary in length from the point at which they are linked to the solid support. Alternatively, heating 2 with an acrylate monomer affords 5 and heating 2 with a styrene monomer affords 6. When the point of attachment of the cyclic nitroxide in the solid-supported initiator is a secondary or tertiary carbon, as is the case for 2, 11, 14, 15, 16 and 17, the polymerization reaction results in solid-supported polymers which have a high degree of monodispersity. Thus, the individual polymer chains of 5 and 6 are similar in length from the point at which they are linked to the solid support.

Furthermore, heating solid-supported initiators with a mixture of monomers as shown in Scheme 4 also provides a compound of Formula I. For example, heating 1 with a mixture of an acrylate monomer and an α -methylstyrene monomer gives 7. Similarly, heating 1 with a mixture of two styrene monomers gives 8. Compounds 7 and 8 contain individual polymer chains that are attached to solid supports which have high polydispersity. Initial heating of 1 with an α -methylstyrene monomer transforms initiator 1 into an initiator which is analogous to 2. Subsequent addition of an acrylate monomer and continued heating affords 9. Similarly, subsequent addition of a styrene monomer affords 10. Both 9 and 10 are solid-supported polymers wherein the individual polymer chains have high monodispersity.

An additional process for preparing a compound of Formula I comprises:

- (1) chemical modification of an insoluble support to covalently attach multiple cyclic nitroxide substituents to the solid support, (2) heating the nitroxide-modified solid support with a substituted styrene or acrylate monomer to grow polymeric chains onto the solid support, (3) rinsing of the solid-supported polymer to remove excess monomer and unattached polymer, (4) heating the resulting solid-supported polymer which still contains cyclic nitroxide moieties with one or more substituted styrene and/or acrylate monomers to extend the polymeric chains, (5) rinsing of the solid-supported polymer to remove excess monomers and unattached polymers, and (6) chemical transformation of functional groups on the polymer as necessary to create a compound of Formula 1 wherein m is an integer from 1 to 100 and q is an

integer from 1 to 300. Illustrative examples of this process are shown in Scheme 6. A solid-supported initiator such as 2 is first heated with styrene to grow polystyrene chains with no crosslinks on the solid support, affording 18. This solid-supported polystyrene is then used as the initiator for subsequent polymerization with
5 functionalized monomers, affording 19 and 20. The effect of this multi-step block polymerization is to extend the desired chemical functionality away from the solid support where it can freely react with reagents in the solution phase. This unique architecture provides solid-supported reagents, solid-supported scavengers and solid phase synthesis supports that exhibit reaction kinetics which more closely
10 resemble the kinetics of analogous chemical reactions in solution.

In the practice of the processes of the present invention, it is often advantageous to remove polymerization inhibitors which are added as preservative to commercial monomers before using these monomers in the methods described above. This may be done through standard means which are known to those skilled
15 in the art of organic synthesis such as, for example, fractional distillation, liquid-liquid extraction, solid-liquid extraction or polymer-supported scavenging and the like. Additionally, the inhibitor may be destroyed *in situ* by addition of at least one molar equivalent of an isocyanate such as, for example, BuNCO, PhNCO and the like per equivalent of inhibitor. The isocyanate reacts with the inhibitor. The
20 resulting inhibitor-isocyanate adducts have no effect on the polymerization process and are easily rinsed away from the desired solid-supported polymers.

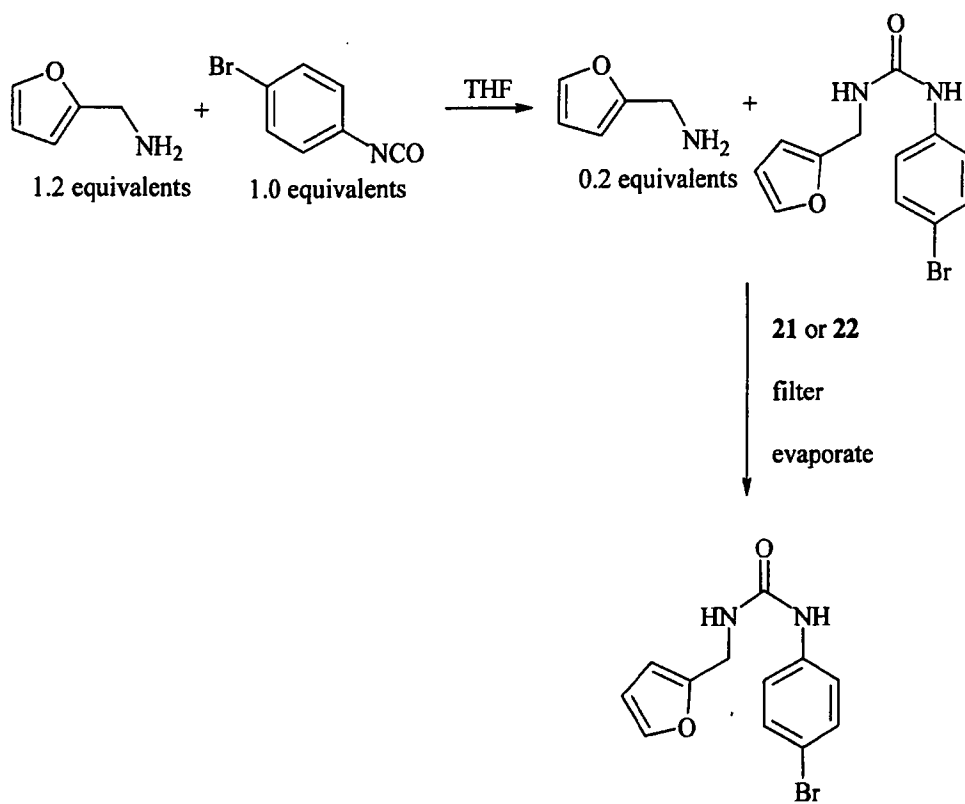
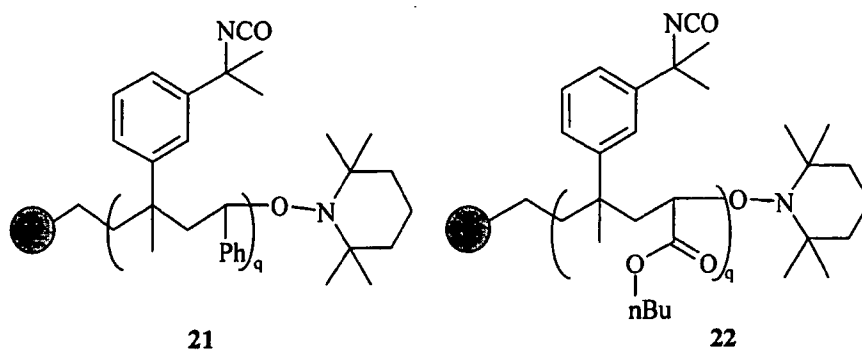
In the practice of the processes of the present invention, the use of an α -methylstyrene monomer along with either an acrylate monomer or a styrene monomer allows efficient synthesis of solid-supported polymers wherein the two
25 monomers tend to alternate, i.e., a compound of Formula I wherein w and p are approximately one is produced. Alternation of the monomers within the solid-supported polymer chains is typically enhanced when the α -methylstyrene monomer composes at least 60 mole percent of the reaction mixture. In cases where both monomers have functionality, this provides a means of alternating two different
30 types of functionality in solid-supported polymers. In cases where only one of the monomers has functionality, this provides a means of modulating the content of functional groups in the solid-supported polymer. When an α -methylstyrene monomer is not one of the monomers, the two types of monomers do not necessarily alternate, i.e., a compound of Formula I wherein w and p are variable is produced.

The third aspect of the present invention is the use of a compound of Formula I, as described above, in solution phase, solid phase organic synthesis or combinatorial chemistry, including use as initiators of solid-supported free-radical polymerization, use as solid-supported scavengers for purification of crude solution phase reaction mixtures, use as a stationary phase for solid phase organic synthesis, and use as solid-supported reagents in solution phase organic synthesis.

Representative descriptions of the use of a compound of Formula I as solid-supported initiators of free radical polymerization are described above and shown in Schemes 3-6. Representative descriptions of the use of a compound of Formula I as solid-supported scavengers, solid-supported reagents, and solid supports for solid phase synthesis are provided in Schemes 7-10. These schemes provide typical examples. All structures in Schemes 3-10 which are numbered by bold arabic numerals are examples of a compound of Formula I.

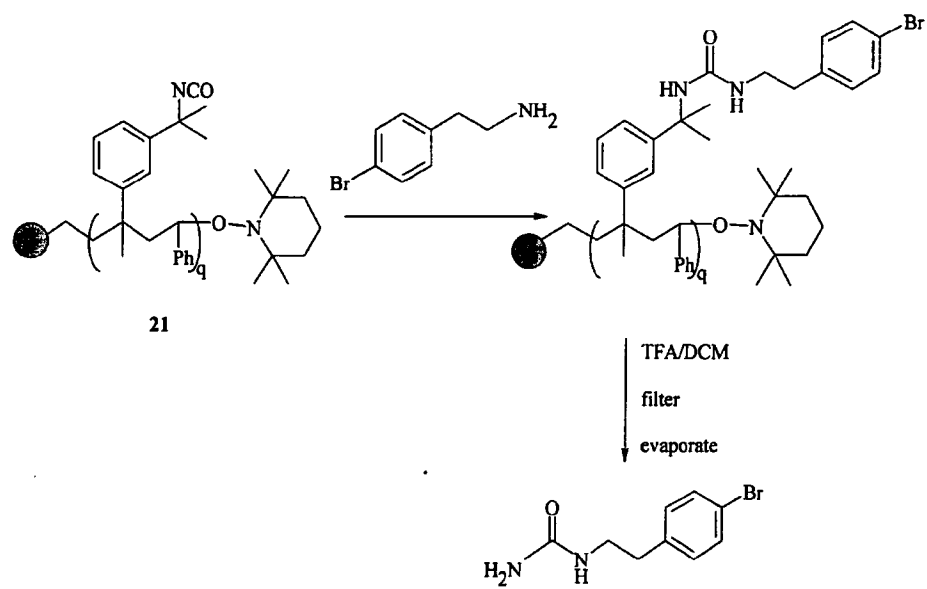
-29-

Scheme 7



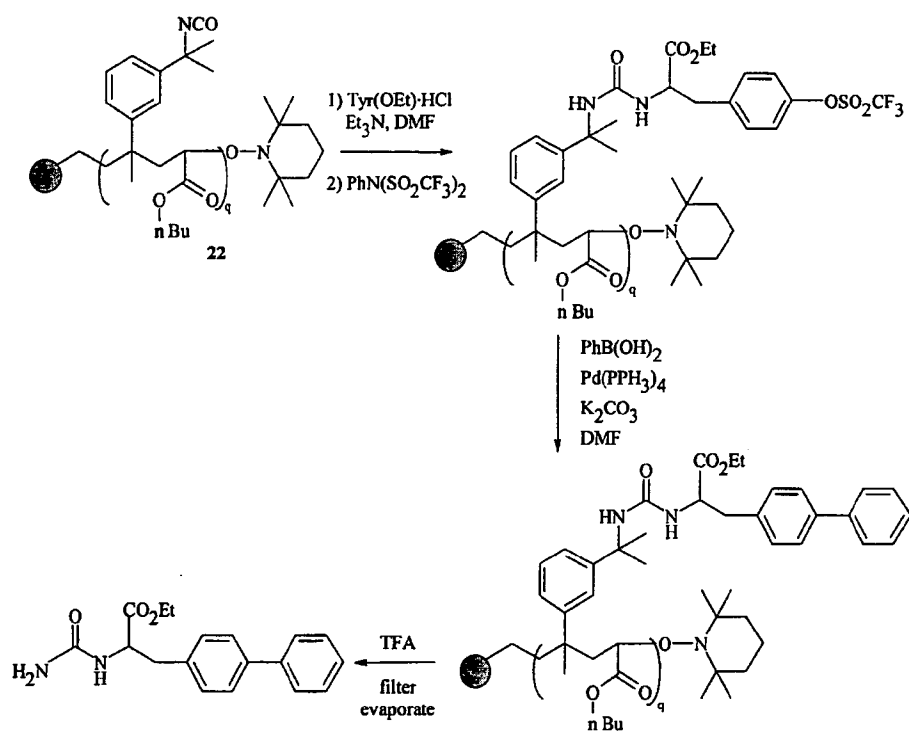
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Scheme 8

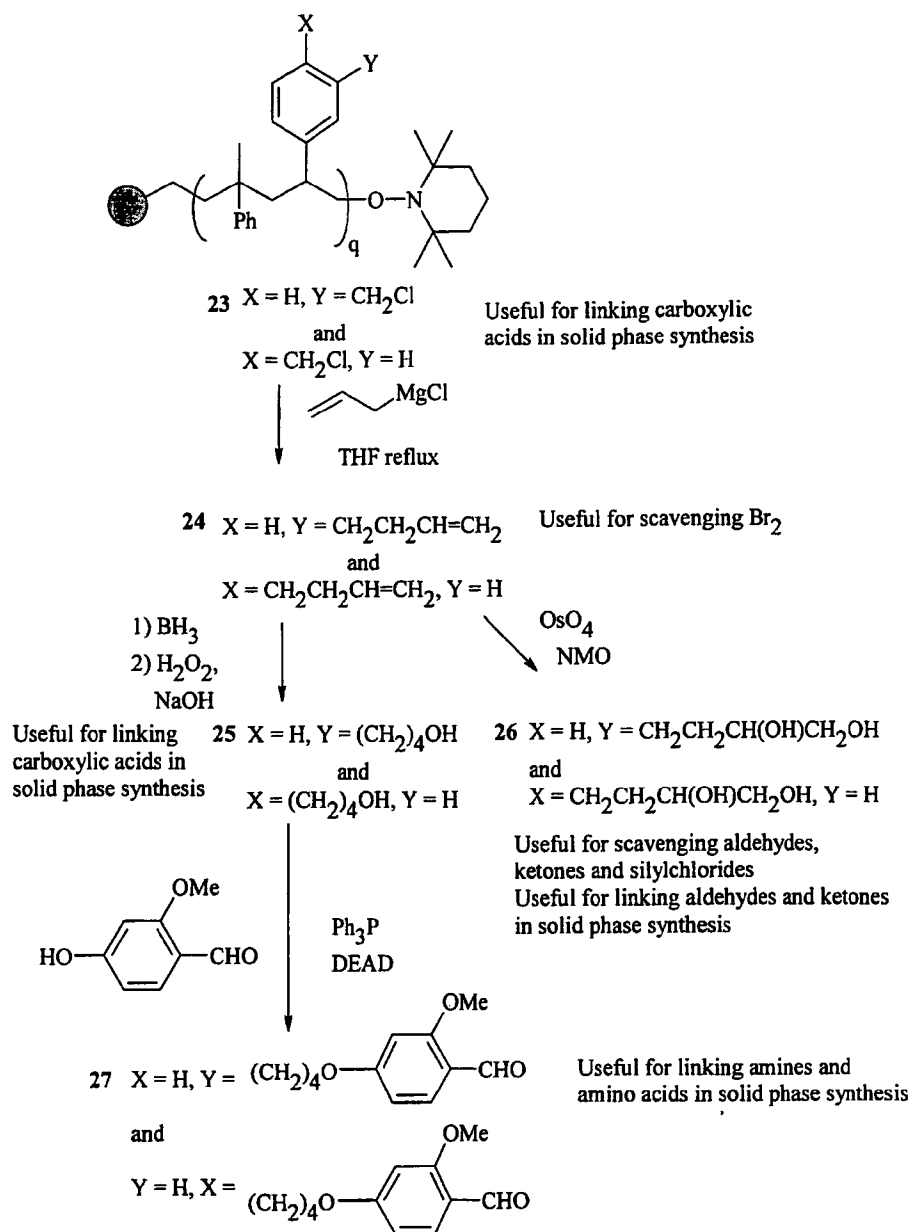


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Scheme 9

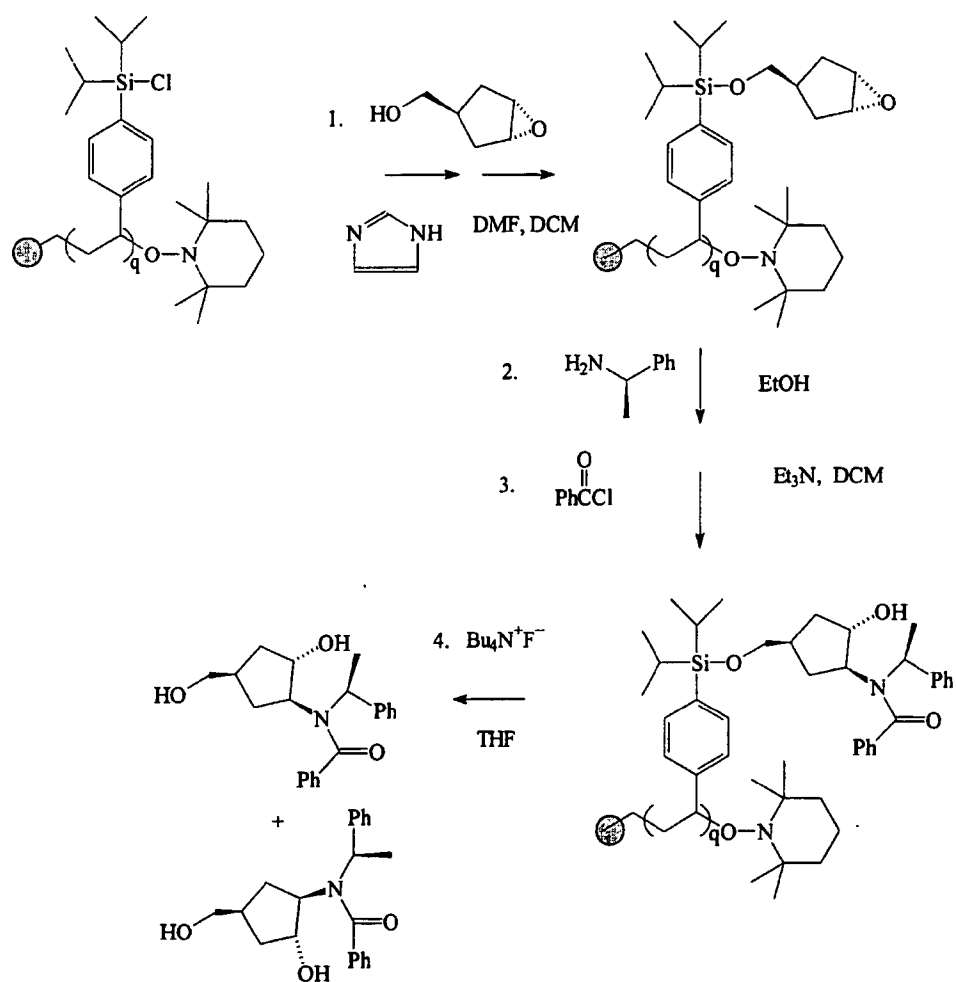


Scheme 10



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Scheme 11



Scheme 7 shows the solid-supported scavenging of excess amine by 21 or 22 which are examples of a compound of Formula I with a high loading of isocyanate groups. Scheme 8 shows the conversion of 2-(4-bromophenyl)-ethylamine to N-(2-(4-bromophenyl)ethyl)urea by treatment with 21, followed by treatment with TFA. Scheme 9 shows a four-step solid phase synthesis of the urea derivative of biphenylalanine, ethyl ester using 22 as the solid support. Scheme 10 shows post polymerization functionality transformations of 23 which lead to 24, 25, 26 and 27 and describes their utilities as solid-supported scavengers and solid supports for solid phase synthesis. Scheme 11 shows a four-step solid phase synthesis of a chiral amide using 28 as the solid support.

The following nonlimiting examples illustrate the inventors' preferred methods for preparing the compounds of the invention.

EXAMPLE 1

TEMPO-methyl-poly(ST-DVB) resin

(A compound of Formula I wherein L is CH₂, m and q are equal to zero, R⁴ is TEMPO.

A solution of sodium ascorbate (12 g, 60 mMol) in water (150 mL) is shaken vigorously with a solution of TEMPO in diethyl ether (125 mL) in a separatory funnel for 10 minutes. The deep red diethyl ether layer turns pale orange. The diethyl ether layer is separated and dried over magnesium sulfate. Reduced pressure concentration on a rotary evaporator at 20°C gives an orange oil. This oil is dissolved in anhydrous DMF (50 mL) and added slowly over 10 minutes to a suspension of NaH (60% dispersion in mineral oil, 1.5 g, 37.5 mMol) in anhydrous DMF (50 mL) under a nitrogen atmosphere. The resulting mixture is stirred 30 minutes more at room temperature, then Merrifield resin (100-200 mesh, 1% DVB, 1.2 mMol Cl/g, 5.0 g, 6 mMol) is added. The resulting slurry is stirred gently for 16 hours at room temperature. The reaction flask is cooled in an ice bath and treated dropwise with cold water (150 mL) while swirling the contents of the flask. The resulting polymeric beads were collected by filtration, washed successively with DMF, H₂O, MeOH, H₂O, H₂O, MeOH, MeOH, DCM, MeOH, DCM, MeOH, DCM, MeOH, DCM, DCM, hexane, hexane, and dried *in vacuo* overnight to afford

5.6 g of a sand colored resin. Found: N, 1.5%; Cl, <0.1%, indicating 1 mMol TEMPO per gram of resin.

EXAMPLE 2

(3-Phenyl-3-TEMPO-butyl)-poly(ST-DVB) resin

5 (A compound of Formula I wherein L is CH₂, m is equal to one, q is equal to zero, R¹ is -CH₂C(CH₃)(Ph)-, R⁴ is TEMPO)

The resin from Example 1 (200 mg, 0.2 mmol N) and MeST (2 mL) are placed in a septum-capped tube. The air in the tube is then purged by pressurizing and venting the tube with nitrogen or argon gas 20 times. The septum-capped tube is then placed in an aluminum block which has been pre-heated to 130°C. Gentle mixing is optionally carried out by orbital shaking. After 12 hours, the tube is cooled to room temperature. The resulting solid beads are collected by filtration and rinsed alternately with dichloromethane and methanol (five cycles of each solvent). After a final wash with methanol, the insoluble beads are dried in a reduced pressure oven at 15 45°C for 6 hours to afford 210 mg of (3-Phenyl-3-TEMPO-butyl)-poly(styrene-divinylbenzene) resin. Calc'd: N, 3.17%. Found: N, 0.94%, indicating 0.27 mMol TEMPO per gram of resin.

EXAMPLE 3

Solid-supported Poly(Br-ST)

20 Method 1: (A compound of Formula I wherein L is CH₂, m and p are zero, w is one, q is an integer from 0 to 200, R² is -CH₂CH(4-bromophenyl)-, R⁴ is TEMPO, and b is 1.0 ± 0.3 mMol of poly (Br-ST) per gram of insoluble solid support.)

4-Bromostyrene (1 mL), containing 10-15 ppm 3,5-di-*t*-butyl catechol as a free radical inhibitor, is treated with 1,5,7-triazabicyclo[4.4.0]dec-5-ene bound to polystyrene crosslinked with 2%DVB (2.2 mMol base/g, 50 mg). The resulting suspension is shaken for 5 minutes at room temperature then filtered. Other standard means of removing the polymerization inhibitor from the monomer such as distillation are equally effective. The resin from Example 1 (50 mg, 50 μMol N) and inhibitor free 4-bromostyrene (0.6 mL, 4.6 mMol) are placed in a septum-capped tube. The air in the tube is then purged by pressurizing and venting the tube with 30

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nitrogen or argon gas 20 times. The septum-capped tube is then placed in an aluminum block which has been pre-heated to 130°C. Gentle mixing is optionally carried out by orbital shaking. After 3 hours, the resulting polymeric mass is cooled to room temperature and treated with dichloromethane (6 mL). The mixture is shaken for about an hour until all of the soluble polymer dissolves. The insoluble beads are collected by filtration and rinsed alternately with dichloromethane and methanol (five cycles of each solvent). After a final wash with methanol, the insoluble beads are dried in a reduced pressure oven at 45°C for 6 hours to afford 470 mg of solid-supported poly(4-bromostyrene). Calc'd: Br, 39.14%. Found: Br, 38.88%. Thus, the solid-supported poly(4-bromostyrene) produced contains 4.86 mMol Br/g.

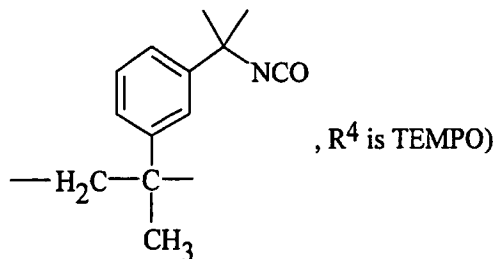
Method 2: (A compound of Formula I wherein L is CH₂, m and o are one, p is zero, q is an integer from 10 to 60, R¹ is -CH₂C(CH₃, Ph)-, R² is -CH₂CH(4-bromophenyl)-, R⁴ is CH₂, and all instances of R⁵ are CH₃)

The resin from Example 2 is used in place of the resin from Example 1 in Method 1 above to afford solid-supported poly(4-bromostyrene).

EXAMPLE 4

(3-(3-(2-Isocyanato-prop-2-yl)phenyl)-3-TEMPO-butyl)-poly(styrene-divinylbenzene) resin

(A compound of Formula I wherein L is CH₂, m is one, q is zero, R¹ is



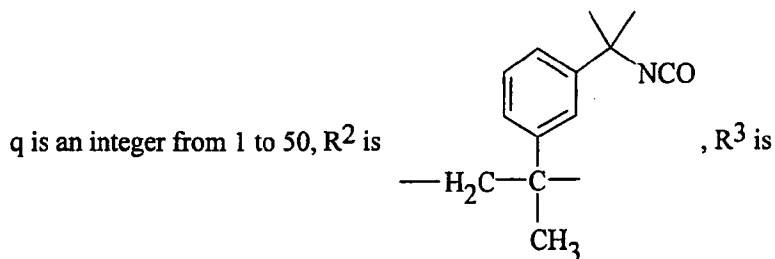
The resin from Example 1 (200 mg, 0.2 mMol) and TMI (2 mL, 10.1 mmol) are placed in a septum-capped tube. The air in the tube is then purged by pressurizing and venting the tube with nitrogen or argon gas 20 times. The septum-

capped tube is then placed in an aluminum block which has been pre-heated to 130° C. Gentle mixing is optionally carried out by orbital shaking. After 18 hours the tube is cooled to room temperature. The beads are then collected by filtration and washed with alternating portions of DCM and hexanes (five times each). After an additional
 5 wash with hexanes, the beads are dried under suction on the filter, then transferred to a vial, and further dried in a reduced pressure oven at 45°C overnight to afford 247 mg. Calc'd: N, 1.67%. Found: N, 1.62%.

EXAMPLE 5

10 Solid-supported Poly(TMI-BA)

Method 1: (A compound of Formula I wherein L is CH₂, m is zero, w and p are one,



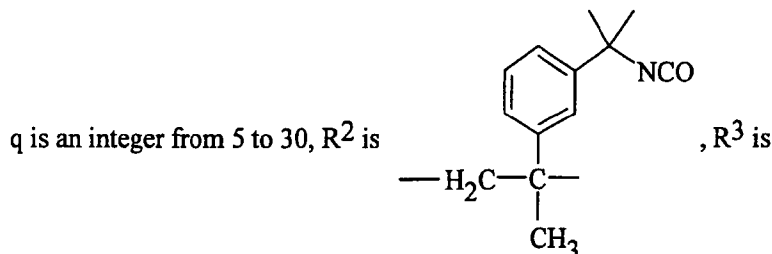
-CH₂CH(CO₂-nBu)-, R⁴ is TEMPO, and b is 1.0 ± 0.3 mMol of poly (TMI-BA) per gram of insoluble solid support.)

15 The resin from Example 1 (400 mg, 0.4 mMol) and a mixture of TMI (3 mL, 15.2 mMol) plus BA (1.4 mL, 9.7 mMol) are placed in a septum-capped tube. The air in the tube is then purged by pressurizing and venting the tube with nitrogen or argon gas 20 times. The septum-capped tube is then placed in an aluminum block which has been pre-heated to 130°C. Gentle mixing is optionally carried out by
 20 orbital shaking. After 18 hours the tube was cooled to room temperature. The resulting wet polymeric mass was treated with DCM (20 mL) and shaken for about 10 minutes to disperse the beads. The beads are then collected by filtration and washed with alternating portions of DCM and hexanes five times. After a final wash with hexanes, the beads are dried under suction on the filter, then transferred to a
 25 vial, and further dried in a reduced pressure oven at 45°C overnight. The yield is

-38-

2.26 g. Found: N, 3.81%, indicating approximately 2.7 mMol NCO/g. IR (KBr) cm^{-1} 2250–2275 (NCO), 1733 ($\text{CO}_2\text{-nBu}$).

Method 2: (A compound of Formula I wherein L is CH_2 , m is zero, w and p are one,



- 5 $\text{-CH}_2\text{CH}(\text{CO}_2\text{-nBu})\text{-}$, R^4 is CH_2 , and all instances of R^5 are CH_3 , and b is 1.0 ± 0.3 mMol of poly (TMI-BA) per gram of insoluble solid support.)

The resin from Example 4 (50 mg, 0.8 mMol N/g) and a mixture of TMI (0.7 mL, 3.5 mmol) plus BA (0.3 mL, 2.1 mMol) are placed in a septum-capped tube. The air in the tube is then purged by pressurizing and venting the tube with
 10 nitrogen or argon gas 20 times. The septum-capped tube is then placed in an aluminum block which has been pre-heated to 130°C . Gentle mixing is optionally carried out by orbital shaking. After 20 hours the tube was cooled to room temperature. The resulting thick slurry was treated with DCM (5 mL) and shaken for about 10 minutes to disperse the beads. The beads are then collected by filtration and
 15 washed with alternating portions of DCM and hexanes (five times each). After an additional wash with hexanes, the beads are dried under suction on the filter, then transferred to a vial, and further dried in a reduced pressure oven at 45°C overnight. The yield is 295 mg. Calc'd: N, 3.91%. Found: N, 3.96%, indicating approximately 2.7 mMol NCO/g. IR (KBr) cm^{-1} 2250–2275 (NCO), 1732 ($\text{CO}_2\text{-nBu}$).

20

EXAMPLE 6

Solid-supported Poly(3-Br-ST)

(A compound of Formula I wherein L is CH_2 , m and p are zero, w is one, q is an integer from 1 to 100, R^2 is $\text{-CH}_2\text{CH}(3\text{-bromophenyl})\text{-}$, R^4 is TEMPO, and b is
 25 0.5 ± 0.28 mMol of poly (3-Br-ST) per gram of insoluble solid support.)

Method 1: (No solvent)

3-Br-ST is distilled on a Kugelrohr apparatus (~1 mmHg, 75–80°C) immediately prior to use. A mixture of resin prepared by the method of Example 1 (0.5 mMol N/g, 100 mg, 50 μ Mol) and 3-Br-ST (0.5 g, 2.73 mMol) is flushed with argon and heated as in Example 3, Method 1. The cooled polymeric mass is treated with DCM (5 mL) and shaken for 90 minutes. The tube was then allowed to stand for 15 minutes. A small quantity of beads float whereas the rest sink. A Pasteur pipet is used to transfer the beads that sink to a filter, adding DCM as necessary to complete the transfer. These beads are then washed with alternating portions of DCM and MeOH (five times each). After one final wash with MeOH, the beads are dried in a reduced pressure oven at 45°C overnight to afford 249 mg of solid-supported poly(3-Br-ST). Found: Br, 30.60%, indicating 3.82 mMol Br/g resin. The floating beads were similarly rinsed and dried to give an additional 20 mg. These had less bromine content. Found: Br, 14.78%, indicating 1.85 mMol Br/g resin.

Method 2: (With solvent)

Method 1 above is repeated with addition of 1,2-dichlorobenzene (125 mg, 0.85 mmol) as solvent. The resulting resin is nearly identical. Sinking portion is 231 mg. Found: Br, 32.19%. Floating portion is 30 mg. Found: Br, 17.17%.

20

EXAMPLE 7

Solid-supported Poly(ClCH₂-ST)

(A compound of Formula I wherein L is CH₂, m and p are zero, w is one, q is an integer from 1 to 100, R² is -CH₂CH (3 and 4-(chloromethyl)phenyl)-, R⁴ is TEMPO, and b is 0.5 \pm 0.28 mMol of poly (ClCH₂-ST) per gram of insoluble solid support.)

A mixture of resin prepared by the method of Example 1 (0.5 mMol N/g, 200 mg, 100 μ Mol) and ClCH₂-ST (a mixture of 3 and 4 isomers, 2.0 mL) is flushed with argon and heated as in Example 3, Method 1. The cooled polymeric mass is refluxed in chloroform (20 mL). The portion of the beads that is easily freed from the mass is collected by filtration and washed with alternating portions of MeOH and DCM (five times each). After a final wash with MeOH, the beads are

dried in a reduced pressure oven to afford 632 mg of solid-supported poly(ClCH₂-ST). Found: Cl, 19.35%, indicating 5.45 mMol Cl/g.

EXAMPLE 8

Solid-supported Poly(HOCH₂-ST)

5 (A compound of Formula I wherein L is CH₂, m and p are equal to zero, w is one, q is an integer from 1 to 100, R² is -CH₂CH(4-(hydroxymethyl)phenyl)-, R⁴ is TEMPO, and b is 0.63 ± 0.28 mMol of poly (HOCH₂-ST) per gram of insoluble solid support.)

10 A mixture of resin prepared by the method of Example 1 (0.63 mMol N/g, 150 mg, 90 μMol) and HOCH₂-ST (a mixture of 3 and 4 isomers, 0.8 mL) is flushed with argon and heated as in Example 3, Method 1. The cooled polymeric mass is shaken with DCM (6 mL) for 1 hour and filtered. The resin beads are washed with alternating portions of MeOH and DCM (five times each). After a final wash with MeOH, the beads are dried in a reduced pressure oven to afford 275 mg
15 of solid-supported poly(HOCH₂-ST). IR (KBr) cm⁻¹ broad, 3200-3500 (OH).

EXAMPLE 9

Solid-supported Poly(BA)

(A compound of Formula I wherein L is CH₂, m and p are zero, w is one, q is an integer from 1 to 40, R² is -CH₂CH(CO₂-nBu)-, R⁴ is TEMPO, and b is 1.0 ± 0.3
20 mMol of poly (BA) per gram of insoluble solid support.)

A mixture of resin from Example 1 (100 mg, 100 μMol), BA (0.6 mL, 4.19 mMol) and BuNCO (0.1 mL, 0.89 mMol) is flushed with nitrogen and heated in a septum capped tube at 130°C for 5 hours. The cooled, wet polymeric mass is mixed with DCM (5 mL) and filtered. The resin beads are washed with alternating
25 portions of MeOH and DCM (five times each). After a final wash with MeOH, the beads are dried in a reduced pressure oven to afford 172 mg of solid-supported poly(BA). IR (KBr) cm⁻¹ 1734 (CO₂-nBu). Found: C, 78.37; H, 8.85; N, 0.81%.

EXAMPLE 10

Solid-supported Poly(BA)-Poly(Br-ST)

(A compound of Formula I wherein L is CH₂, m is an integer from 1 to 40, p is zero,

q is an integer from 1 to 100, R¹ is -CH₂CH(CO₂-nBu)-, R² is

5 -CH₂CH(4-bromophenyl)-, R⁴ is TEMPO, and b is 1.0 ± 0.3 mMol of poly (BA)-poly(Br-ST) per gram of insoluble solid support.)

A mixture of resin from Example 10 (50 mg, 29 μMol N) and inhibitor free Br-ST (see Example 3, 0.6 mL, 4.6 mMol) is flushed with nitrogen and heated in a septum capped tube at 130°C for 18 hours. The cooled polymeric mass is shaken
10 with DCM (5 mL) for 4 hours then filtered. The resulting resin beads are washed with alternating portions of DCM and MeOH (five times each). After a final wash with MeOH, the beads are dried in a reduced pressure oven to afford 499 mg of solid-supported poly(BA)-poly(Br-ST). IR (KBr) cm⁻¹ 1731 (CO₂-nBu). Found: Br, 40.18%, indicating 5.0 mMol Br/g.

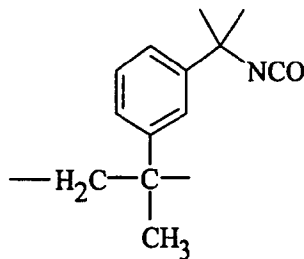
15

EXAMPLE 11

Solid-supported Poly(TMI-ST)

(A compound of Formula I wherein L is CH₂, m is zero, w and p are one, q is an

integer from 3 to 30, R² is



, R³ is -CH₂CH(Ph)-, R⁴ is

TEMPO, and b is 1.0 ± 0.3 mMol of poly (TMI-ST) per gram of insoluble solid
20 support.)

Resin from Example 1 (200 mg, 0.2 mMol N) and TMI (2 mL, 10.1 mMol) are placed in a septum-capped tube, and the tube is flushed with nitrogen. The capped tube is heated at 130°C for 18 hours, then cooled to room temperature. ST (0.5 mL, 4.4 mMol) is then added, and the tube is flushed with nitrogen. The capped
25 tube is then reheated at 130°C for 24 hours. After cooling to room temperature, the

resulting wet polymeric mass is mixed with DCM (5 mL), and the resin beads are collected by filtration. The beads are rinsed with alternating portions of DCM and hexanes (five times each). Drying in a reduced pressure oven at 45°C for 24 hours affords 830 mg of solid-supported poly(TMI-ST). IR (KBr) cm⁻¹ 2250-2275 (NCO).

EXAMPLE 12

Scavenging Capacity of Solid-supported Polymers Bearing NCO Groups

Resins from Examples 5 and 11 (50 mg, ~0.1 to 0.15 mMol NCO) are swelled in DCM (0.9 mL) and treated with 2-(4-bromophenyl)-ethylamine (0.1 mL, 0.64 mMol). The resulting mixtures are shaken in a capped vial for 18 hours at room temperature. The resins are filtered and rinsed with alternating portions of DCM and MeOH (five times each). After an additional wash with MeOH, the resins are dried in a reduced pressure oven at 45°C overnight to afford the corresponding urea resins. The following results were observed:

Urea resin derived from resin of Example 5, Method 1: Br, 15.77%.
Urea resin derived from resin of Example 5, Method 2: Br, 16.16%.
Urea resin derived from resin of Example 11: Br, 17.48%.

These results are consistent with a maximum amine scavenging capacity of ~3 mMol/g for solid-supported poly(TMI-BA) of Example 5 and for solid-supported poly(TMI-ST) of Example 11.

EXAMPLE 13

Conversion of N-(2-(4-bromophenyl)-ethyl)amine to N-(2-(4-bromophenyl)-ethyl)urea

(Use of a compound of Formula 1 in a solid phase synthesis)

Solid supported poly(TMI-BA) from Example 5 (50 mg) is reacted with excess 2-(4-bromophenyl)ethylamine and the resin is washed as in Example 12. The resulting urea resin is treated with TFA-d (0.5 mL) and shaken in a capped vial for 2 hours at room temperature. The red colored resin is removed by filtration, and a proton NMR spectrum and a mass spectrum are obtained from the filtrate. ¹H-NMR (TFA-d) δ 7.45 (d, 2H, Ar-H), 7.12 (d, 2H, Ar-H). 3.64 (t, 2H, CH₂N), 2.95 (t, 2H, CH₂Ar). MS (AP+, MeCN-H₂O) 243/245 (m+1), 284/286 (m+MeCN+1). Spectral

data are in agreement with N-(2-(4-bromophenyl)-ethyl)urea. The absence of other resonances in the NMR spectrum indicates high purity.

EXAMPLE 14

Solid-supported Poly(MeST-ClCH₂-ST))

- 5 (A compound of Formula I wherein L is CH₂, m is zero, w and p are one, q is an integer from 1 to 40, R² is -CH₂C(CH₃, Ph)-, R³ is -CH₂CH(3- and 4-(chloromethyl)phenyl)-, R⁴ is TEMPO, and b is 1.0 ± 0.3 mMol of poly (MeST-ClCH₂-ST) per gram of insoluble solid support.)

- 10 A mixture of resin prepared by the method of Example 1 (1.0 mMol N/g, 200 mg, 200 μMol), MeST (1.5 mL, 11.5 mMol) and ClCH₂-ST (a mixture of 3 and 4 isomers, 0.75 mL, 5.28 mMol) is flushed with nitrogen and heated in a capped vial at 130°C for 18 hours. The cooled slurry is diluted with DCM and filtered, and the polymer beads are washed with alternating portions of MeOH and DCM (five times each). After a final wash with MeOH, the beads are dried in a
15 reduced pressure oven to afford 468 mg of solid-supported poly(MeST-ClCH₂-ST). Found: Cl, 9.66%, indicating 2.7 mMol Cl/g.

EXAMPLE 15

Solid-supported Poly(MeST-(3- and 4-(3-buten-1-yl)-ST)))

- 20 (A compound of Formula I wherein L is CH₂, m is zero, w and p are one, q is an integer from 1 to 40, R² is -CH₂C(CH₃, Ph)-, R³ is -CH₂CH(3- and 4-(3-buten-1-yl)phenyl)-, R⁴ is TEMPO, and b is 1.0 ± 0.3 mMol of poly (MeST-(3- and 4-(3-buten-1-yl)-ST))) per gram of insoluble solid support.)

- 25 Resin from Example 14 (0.185 g, 0.5 mmol) is treated with a solution of allylmagnesium chloride (4.0 mL of 2.0 M solution in THF, 8.0 mmol) under nitrogen. The reaction mixture is then refluxed gently for 20 hours after which the reaction mixture is cooled, and the resin is collected by filtration (the filtrate is quenched carefully with cold water). The resin is washed successively with 3 × THF, 3 × THF: H₂O(1:1), 3 × H₂O, 3 × 1N HCl : THF(1:1), 3 × THF: H₂O(1:1), 3 × H₂O, 3 × THF: H₂O(1:1), 3 × THF. The washed resin is dried in *in vacuo* at room

-44-

temperature overnight, to obtain a colorless resin (0.184 g). Found: Cl, <0.1%. IR (KBr) cm^{-1} 1639 (C=C).

EXAMPLE 16

Bromine Scavenging

- 5 A solution of bromine (0.5 mMol) in DCM (5 mL) is chilled in an ice bath, treated with the resin from Example 15 (100 mg) and shaken for 15 minutes. The solution becomes colorless and the resin takes on a yellow color. Filtration of the polymer beads gives a colorless filtrate that yields no residue upon evaporation.

EXAMPLE 17

10 Solid-supported Poly(MeST-(3- and 4-(4-hydroxybutyl-ST)))

(A compound of Formula I wherein L is CH_2 , m is zero, w and p are one, q is an integer from 1 to 40, R^2 is $-\text{CH}_2\text{C}(\text{CH}_3, \text{Ph})-$, R^3 is $-\text{CH}_2\text{CH}(3-$ and $4-(4-$ hydroxybutyl)phenyl)-, R^4 is TEMPO, and b is 1.0 ± 0.3 mMol of poly (MeST-(3- and 4-(4-hydroxybutyl-styrene))) per gram of insoluble solid support.)

- 15 To the alkene functionalized resin from Example 15 (0.025g, ~0.06 mMol) under nitrogen is added 9-BBU (2.0 mL of 0.5 M solution in THF, 1.0 mmol). The resulting slurry is stirred for 3 hours at room temperature, then the resin was filtered and washed with THF (3 \times). The resin is suspended in THF (20 mL) and treated with methanolic tetrabutylammonium hydroxide (2 mL of a 1 M solution, 1 mMol),
20 followed by aqueous hydrogen peroxide (0.7 mL of 30% solution, ~6 mMol). The resulting mixture is stirred at room temperature for 3 hours. The resin beads are collected by filtration, washed with 3 \times THF, 3 \times THF: $\text{H}_2\text{O}(1:1)$, 3 \times H_2O , 3 \times MeOH, 3 \times THF, and dried *in vacuo* to afford a colorless resin (0.86 g). IR (KBr) cm^{-1} broad, 3200–3500 (OH).

25

EXAMPLE 18

Solid-supported Poly(4-(1-isocyanatoethyl)styrene)

(A compound of Formula I wherein L is CH_2 , m and p are zero, w is one, q is an integer from 1 to 100, R^2 is $-\text{CH}_2\text{CH}(4-(1-\text{isocyanatoethyl})\text{phenyl})-$, R^4 is

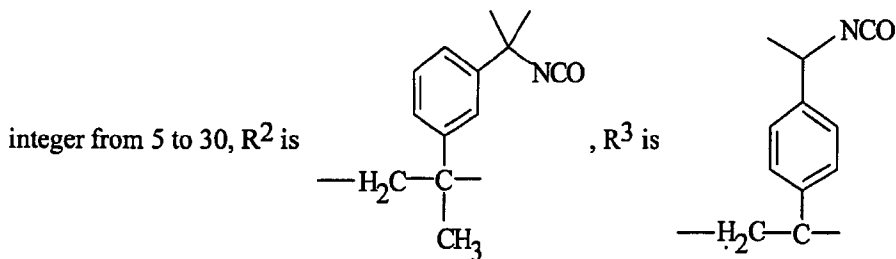
TEMPO, and b is 1.0 ± 0.3 mMol of poly (TMI-BA) per gram of insoluble solid support.)

The resin from Example 1 (50 mg, 50 μ Mol N) and 4-(1-isocyanatoethyl)styrene (865 mg, 5 mMol) are placed in a septum-capped tube. The air in the tube is then purged by pressurizing and venting the tube with nitrogen or argon gas 20 times. The septum-capped tube is then placed in an aluminum block which has been pre-heated to 130°C. Gentle mixing is optionally carried out by orbital shaking. After 8 hours, the resulting polymeric mass is cooled to room temperature and treated with dichloromethane (6 mL). The mixture is shaken for about an hour until all of the soluble polymer dissolves. The insoluble beads are collected by filtration and subsequently rinsed alternately with dichloromethane and hexanes (five cycles of each solvent). After a final wash with hexanes, the insoluble beads are dried in a reduced pressure oven at 45°C for 6 hours to afford 400 mg of solid-supported poly(4-(1-isocyanatoethyl)styrene) which contains 5.0 mMol NCO/g.

EXAMPLE 19

Solid-supported Poly(TMI-(4-(1-isocyanatoethyl)styrene))

(A compound of Formula I wherein L is CH₂, m is zero, o and p are one, q is an



R⁴ is TEMPO, and b is 1.0 ± 0.3 mMol of poly (TMI-(4-(1-isocyanatoethyl)styrene)) per gram of insoluble solid support.)

Resin from Example 1 (200 mg, 0.2 mMol N) and TMI (2 mL, 10.1 mMol) are placed in a septum-capped tube, and the tube is flushed with nitrogen. The capped tube is heated at 130°C for 18 hours, then cooled to room temperature. 4-(1-Isocyanatoethyl)-styrene (760 mg, 4.4 mMol) is then added, and the tube is flushed with nitrogen. The capped tube is then reheated at 130°C for 24 hours. After

cooling to room temperature, the resulting wet polymeric mass is mixed with DCM (5 mL), and the resin beads are collected by filtration. The beads are rinsed with alternating portions of DCM and hexanes (five times each). Drying in a reduced pressure oven at 45°C for 24 hours affords 850 mg of solid-supported poly(TMI-(4-(1-isocyanatoethyl)styrene)) containing 4 mmol NCO/g.

EXAMPLE 20

General Procedure for Preparing *p*-dialkylsilane styrenes

To an oven-dried 250 mL round-bottom flask, equipped with stir bar and cooled/purged under a stream of N₂ gas, was placed dry Et₂O (150 mL, 0.2 M) and cooled to -78°C. *tert*-Butyllithium (39 mL, 1.7 M, 66 mmol) was added via syringe, followed by the dropwise syringe addition of *p*-bromostyrene (4.33 mL, 33 mmol). The solution rapidly changed from bright red to a deep orange hue. After 20 minutes at -78°C, a dialkylchlorosilane (33 mmol) was added dropwise via syringe. The bath was removed, and the reaction was allowed to slowly warm to RT. The color lightened to a pale yellow, and the salts precipitated out after 2 hours. The reaction was then quenched with water, extracted into hexanes and washed with brine. Concentration *in vacuo* and column chromatography [98% hexanes, 2% Et₃N] affords the dialkylsilane styrene

H-DIPS-ST Obtained was 6.6 g (92%) of a water-white oil. TLC [hexanes] R_f=0.85; IR (thin film) cm⁻¹: 2101(s, Si-H), 1462. ¹H NMR (400 MHz, CDCl₃): Δ 7.46 (d, *J*=8 Hz, 2H), 7.37 (d, *J*=8 Hz, 2H), 6.69 (dd, *J*= 10.9, 17.5 Hz, 1H), 5.77 (d, *J*=17.5 Hz, 1H), 5.24 (d, *J*=17.5 Hz, 1H), 3.91 (m, 1H), 1.2 (m, 2H), 1.04 (d, *J*=7.3 Hz, 6H), 0.97 (d, *J*=7.3 Hz, 6H).

EXAMPLE 21

Solid-supported Poly(H-DIPS-ST)

(A compound of Formula I wherein L is CH₂, m and p are zero, w is one, qu is an integer from 1 to 100, R² is -CH₂CH(4-(diisopropylsilyl)phenyl)-, R⁴ is TEMPO and b is 1.0 ± 0.3 mMol of poly (H-DIPS-ST) per gram of insoluble solid support.

A suspension of resin from Example 1 (100 mg, 1.0 mMol/g, 0.10 mMol) in H-DIPS-ST (980 mg, 4.5 mMol, 45 molar excess) was heated at 130°C for 20 hours in a capped vial under an atmosphere of N₂. After cooling, the polymeric mass was diluted with DCM and the resin beads collected by filtration. Washing with DCM

then methanol (5 cycles) followed by drying in a vacuum oven at 50°C afforded, 500 mg of solid-supported poly (H-DIPS-ST) as large, white beads. IR cm^{-1} : 2101 (s, Si-H). Found: Si, 6.4% which correlates to a loading of 2.3 mMol Si per gram of resin.

5

EXAMPLE 22

Solid-supported Poly(Cl-DIPS-ST)

(A compound of Formula I wherein L is CH_2 , m and p are zero, w is one, q is an integer from 1 to 100, R^2 is $-\text{CH}_2\text{CH}(4-(\text{diisopropyl-chlorosilyl})\text{phenyl})-$, R^4 is TEMPO and b is 1.0 ± 0.3 mMol of poly(Cl-DIPS-ST) per gram of insoluble solid support.

A portion of the resin from Example 21 (300 mg, 0.69 mMol) were placed in a dry 100 mL solid-phase peptide reaction vessel, cooled and purged under an atmosphere of N_2 , and 1,3-dichloro-5,5-dimethylhydantoin (408 mg, 2.07 mMol, 15 3.0 equiv.) was added. Dry DCM (8 mL) was subsequently added, the vessel was placed on an orbital stirrer and the reaction was agitated at room temperature for 3 hours. After this time, the resin was filtered under N_2 and washed with dry THF (3 x 20 mL) and DCM (3 x 20 mL) to remove the excess 1,3-dichloro-5,5-dimethylhydantoin to afford solid-supported poly(Cl-DIPS-ST). IR: Shows no peak 20 at 2101 cm^{-1} indicating complete conversion of Si-H to Si-Cl.

EXAMPLE 23

Solid-supported Poly(Me-ST-(H-DIPS-ST))

(A compound of Formula I wherein L is CH_2 , m is zero, w and p are one, q is an integer from 1 to 50, R^2 is $-\text{CH}_2\text{C}(\text{CH}_3, \text{Ph})-$, R^3 is $-\text{CH}_2\text{CH}(4-$ 25 $\text{diisopropylsilyl})\text{phenyl})-$, R^4 is TEMPO and b is 1.0 ± 0.3 mMol of poly(Me-ST-(H-DIPS-ST) per gram of insoluble solid support.

Resin from Example 1 (100 mg, 1.0 mmol/g, 0.10 mmol) in a mixture (45 molar excess) of H-DIPS-ST (from Example 20, 349 mg, 1.6 mmol) and Me-ST 30 (342 mg, 2.9 mmol) was heated at 130°C for 20 hours in a capped vial under an atmosphere of N_2 . After cooling, the polymeric mass was diluted with DCM and the resin beads collected by filtration. Washing with DCM then methanol (5 cycles) followed by drying in a vacuum oven at 50°C afforded 471 mg of solid-supported poly(Me-ST-(H-DIPS-ST)) as large, white beads. IR (KBr pellet) cm^{-1} : 2098(s,

Si-H).

EXAMPLE 24

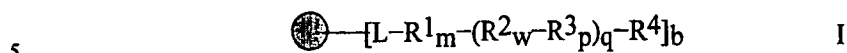
Solid-supported Poly(F₅-ST)

5 (A compound of Formula I wherein L is CH₂, m and p are zero, w is one, q is an integer from 1 to 100, R² is -CH₂CH(2,3,4,5-pentafluorophenyl)-, R⁴ is CH₂, all instances of R⁵ are CH₃, and b is 0.5 ± 0.28 mMol of poly (F₅-ST) per gram of insoluble solid support.)


10 A mixture of resin from Example 1 (1 mMol N/g, 150 mg, 150 μMol), F₅-ST (2.5 mL, 18 mMol) and *m*-tolyl isocyanate (75 μL, 570 μMol) is flushed with nitrogen and heated at 130°C for 17.5 hours. The cooled polymeric mass is treated with DCM (6 mL) and shaken for 10 minutes. The suspension of beads is filtered and the beads are then washed with alternating portions of DCM and MeOH (five times each). After one final wash with MeOH, the beads are dried in a reduced
15 pressure oven at 45–50°C overnight to afford 1.97 g of solid-supported poly(F₅-ST). Found: F 44.83% indicating 23 mMol F/g resin.

CLAIMS

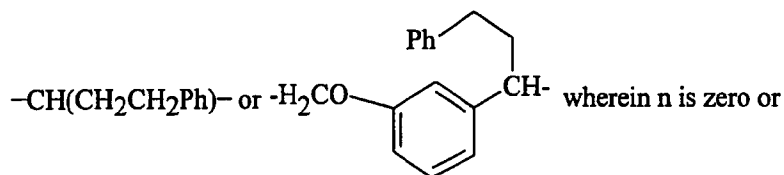
1. A compound of Formula I



wherein

 is an insoluble solid support selected from the group consisting of
poly(styrene-divinylbenzene), macroreticular poly(styrene-
divinylbenzene), polystyrene which is radiation grafted to
10 polypropylene, polystyrene which is radiation grafted to polyethylene,
polystyrene which is radiation grafted to poly(tetrafluoroethylene) and
polystyrene which is radiation grafted to poly(ethylene-
tetrafluoroethylene) wherein the insoluble solid support is in a shape
selected from a bead, a tube, a rod, a ring, a disk or a well;

15 L is $-\text{CH}_2-$, $-\text{C}(\text{CH}_3)_2-$, $-\text{CH}(\text{CH}_3)-$, $-(\text{CH}_2)_n\text{CH}(\text{CN})-$,
 $-(\text{CH}_2)_n\text{CH}(\text{CO}_2\text{Me})-$, $-(\text{CH}_2)_n\text{CH}(\text{Ph})-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3, \text{Ph})-$,



an integer from 1 to 5;

m is zero or an integer from 1 to 100;

20 w is zero or an integer from 1 to 10;

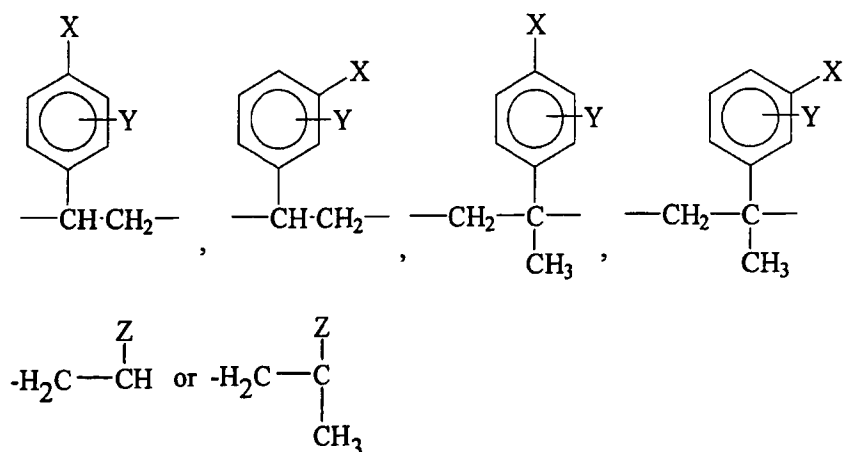
p is zero or an integer from 1 to 10;

q is zero or an integer from 1 to 300;

b is mMol content of initiator or solid-supported polymer per gram of
insoluble solid support and is about 0.1 to about 5.0 mMol per gram;

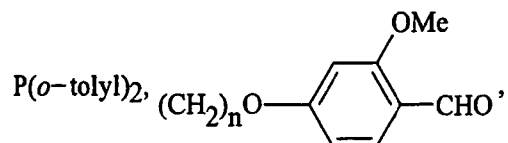
25 R^1 , R^2 and R^3 are each independently the same or different and are:

-50-

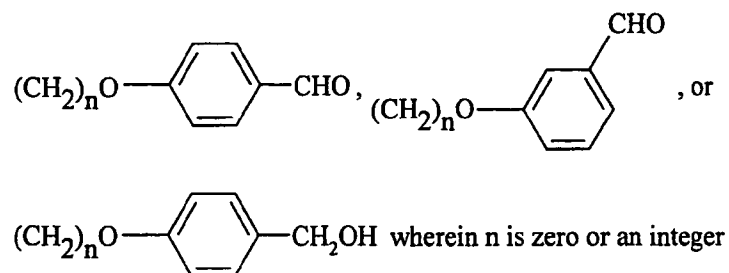


wherein

X is H, F, $(\text{CH}_2)_n\text{Cl}$, $(\text{CH}_2)_n\text{Br}$, $(\text{CH}_2)_n\text{I}$, $\text{B}(\text{OH})_2$, $(\text{CH}_2)_n\text{CH}=\text{CH}_2$, NCO ,
 5 CH_2NCO , $\text{CH}(\text{CH}_3)\text{NCO}$, $\text{C}(\text{CH}_3)_2\text{NCO}$, CO_2Me , CO_2Et , $\text{CO}_2(t\text{-Bu})$, CO_2H , COCl , $\text{CO}_2\text{CH}(\text{CF}_3)_2$, CO_2Ph ,
 $\text{CO}_2(\text{pentafluorophenyl})$, $\text{CO}_2(\text{pentachlorophenyl})$,
 $\text{CO}_2(\text{N-succinimidy})$, $\text{C}(\text{OMe})_3$, $\text{C}(\text{OEt})_3$, $(\text{CH}_2)_n\text{OH}$,
 $(\text{CH}_2)_n\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $(\text{CH}_2)_n\text{SH}$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{SH}$,
 10 $\text{CH}_2)_n\text{NHC}(=\text{S})\text{NH}_2$, $(\text{CH}_2)_n\text{NH}_2$, $(\text{CH}_2)_n\text{N}(\text{Me})_2$, $(\text{CH}_2)_n\text{N}(\text{Et})_2$,
 $(\text{CH}_2)_n(i\text{Pr})_2$, $\text{CH}(\text{CH}_3)\text{NH}_2$, $\text{C}(\text{CH}_3)_2\text{NH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$,
 $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$,
 $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$,
 $(\text{CH}_2)_n(\text{morpholin-4-yl})$, $(\text{CH}_2)_n(\text{piperidin-1-yl})$,
 15 $(\text{CH}_2)_n(4\text{-methypiperazin-1-yl})$, $\text{N}(\text{SO}_2\text{CF}_3)_2$, $(\text{CH}_2)_n\text{CHO}$,
 $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(i\text{Pr})_2\text{H}$,
 $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(i\text{-Pr})_2\text{Cl}$,
 $(\text{CH}_2)_n\text{Si}(t\text{Bu})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Ph})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Ph})(t\text{Bu})\text{Cl}$, $\text{P}(\text{Ph})_2$,



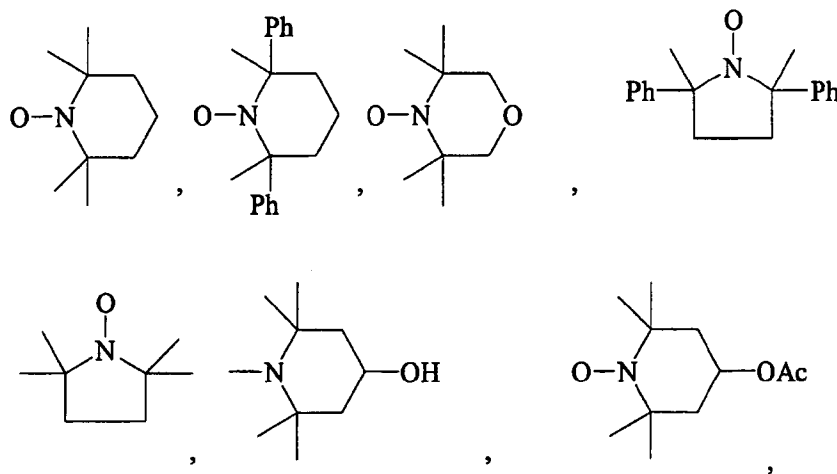
-51-



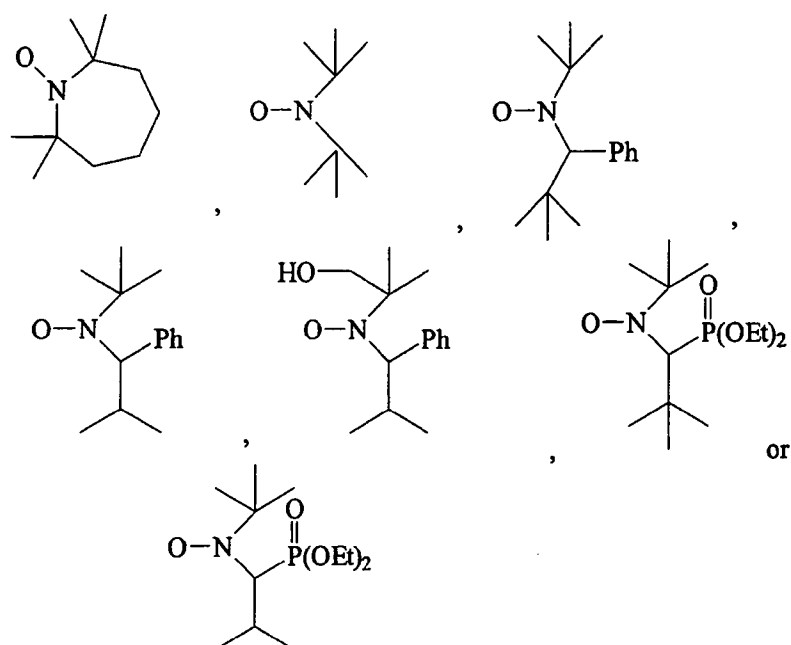
from 1 to 5;



Y is H, Cl, Br, F, OH, or OMe;

5 Z is NCO, CO₂Me, CO₂Et, CO₂(*i*-Pr), CO₂(*n*-Bu), CO₂(*t*-Bu), CN,
 CO₂H, COCl, CO₂CH(CF₃)₂, CO₂(pentafluorophenyl),
 CO₂(pentachlorophenyl), CO₂Ph, CO₂(N-succinimidyl), C(OMe)₃,
 C(OEt)₃, CON(OCH₃)CH₃, CHO, CH₂OH, or C(CH₃)₂OH;

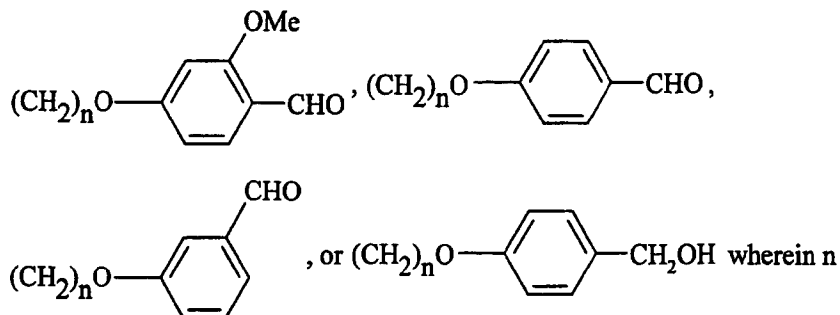
R⁴ is

-52-



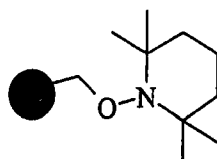
2. The compound according to Claim 1 wherein  is an insoluble solid support selected from the group consisting of: poly(styrene-divinylbenzene) and macroreticular poly(styrene-divinylbenzene) in the shape of a bead.
3. The compound according to Claim 1 wherein  is an insoluble solid support selected from the group consisting of: polystyrene which is radiation grafted to polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene) and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) in the shape selected from a tube, a rod, a ring, a disk, or a well.
4. The compound according to Claim 1 wherein L is $-\text{CH}_2-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3)\text{Ph}-$, or $-\text{CH}(\text{CH}_2\text{CH}_2\text{Ph})-$.
5. The compound according to Claim 1 wherein m and q are equal to zero.


6. The compound according to Claim 1 wherein m is equal to zero, and q is an integer from 1 to 300.
7. The compound according to Claim 1 wherein m is an integer from 1 to 100, and q is an integer from 1 to 300.
- 5 8. The compound according to Claim 1 wherein X is NCO, CH₂NCO, CH(CH₃)NCO, or C(CH₃)₂NCO, and Y is H.
9. The compound according to Claim 1 wherein X is (CH₂)_nNH₂, (CH₂)_nN(Me)₂, (CH₂)_nN(Et)₂, (CH₂)_n(iPr)₂, CH(CH₃)NH₂, C(CH₃)₂NH₂, CH₂NHCH₂CH₂NH₂, CH₂NHCH₂CH₂NHCH₂CH₂NH₂,
 10 CH₂N(CH₂CH₂NH₂)₂, CH₂NHCH₂CH₂N(CH₂CH₂NH₂)₂, CH₂N(CH₂CH₂OH)₂, (CH₂)_n(morpholin-4-yl), (CH₂)_n(piperidin-1-yl), or (CH₂)_n(4-methylpiperazin-1-yl) wherein n is zero or an integer from 1 to 5.
10. The compound according to Claim 1 wherein X is (CH₂)_nSH,
 15 CH₂NHCH₂CH₂SH, or CH₂)_nNHC(=S)NH₂ wherein n is zero or an integer from 1 to 5.
11. The compound according to Claim 1 wherein X is (CH₂)_nCl, (CH₂)_nBr, (CH₂)_nI, (CH₂)_nOH, or (CH₂)_nCH(OH)CH₂OH wherein n is zero or an integer from 1 to 5.
- 20 12. The compound according to Claim 1 wherein X is



is zero or an integer from 1 to 5.

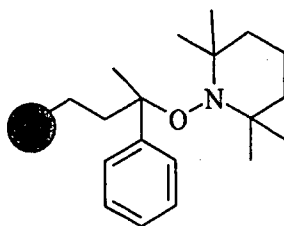
13. The compound according to Claim 1 wherein X is CO₂Me, CO₂Et, CO₂(*t*-Bu), CO₂H, COCl, CO₂CH(CF₃)₂, CO₂Ph, CO₂(pentafluorophenyl), CO₂(pentachlorophenyl), CO₂(N-succinimidyl), C(OMe)₃, or C(OEt)₃.
- 5 14. The compound according to Claim 1 wherein X is (CH₂)_nSi(Me)₂H, (CH₂)_nSi(Et)₂H, (CH₂)_nSi(*i*Pr)₂H, (CH₂)_nSi(*t*Bu)₂H, (CH₂)_nSi(Ph)₂H; (CH₂)_nSi(Ph)(*t*Bu)H, (CH₂)_nSi(Me)₂Cl; (CH₂)_nSi(Et)₂Cl, (CH₂)_nSi(*i*Pr)₂Cl, (CH₂)_nSi(*t*Bu)₂Cl, (CH₂)_nSi(Ph)₂Cl or (CH₂)_nSi(Ph)(*t*Bu)Cl.
- 10 15. The compound according to Claim 1 wherein Z is NCO, CO₂Me, CO₂Et, CO₂(*i*-Pr), CO₂(*n*-Bu), CO₂(*t*-Bu), CN, CO₂H, COCl, CO₂CH(CF₃)₂, CO₂(pentafluorophenyl), CO₂(pentachlorophenyl), CO₂Ph, CO₂(N-succinimidyl), C(OMe)₃, C(OEt)₃, CON(OCH₃)CH₃, CHO, CH₂OH, or C(CH₃)₂OH.
16. The compound according to Claim 1 wherein R⁴ is CH₂, and R⁵ is CH₃.
- 15 17. The compound according to Claim 1 which is




wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, and the nitrogen content is 0.1 to 4 mMol per gram.

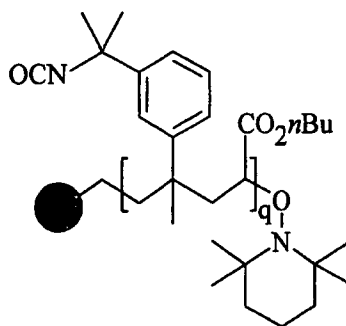
- 20 18. The compound according to Claim 1 which is


-55-



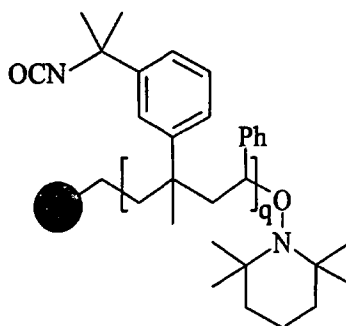
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, and the nitrogen content is 0.1 to 4 mMol per gram.


- 5 19. The compound according to Claim 1 which is



wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30 and the isocyanate content is 1 to 4 mMol per gram.

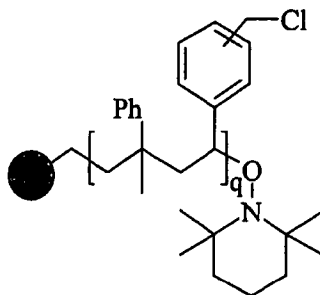
- 10 20. The compound according to Claim 1 which is




wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30 and the isocyanate content is 1 to 4 mMol per gram.

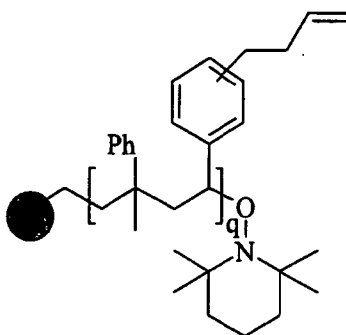
-56-


21. The compound according to Claim 1 which is



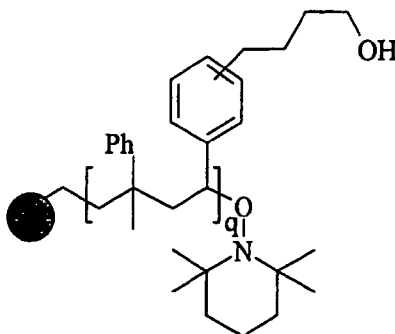
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the chlorine content is 1 to 4 mMol per gram.

22. The compound according to Claim 1 which is



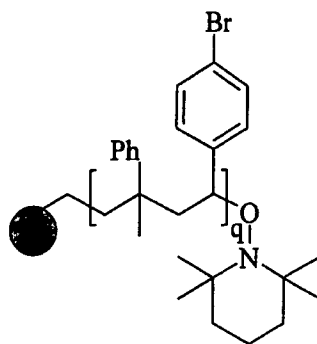
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the alkene content is 1 to 4 mMol per gram.

23. The compound according to Claim 1 which is



wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the hydroxyl content is 1 to 4 mMol per gram.

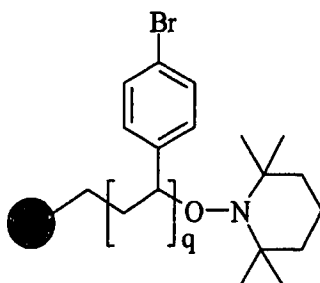
24. The compound according to Claim 1 which is



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wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the bromine content is 1 to 4 mMol per gram.

25. The compound according to Claim 1 which is

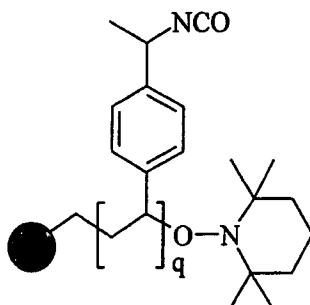



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wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 80 with an average of between 10 and 60, and the bromine content is 1 to 6 mMol per gram.

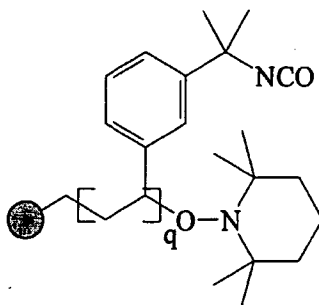
-58-


26. The compound according to Claim 1 which is



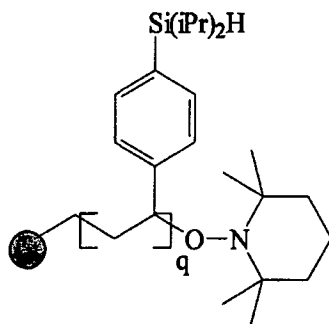
wherein  is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 80 with an average of between 10 and 60, and the isocyanate content is 1 to 6 mMol per gram.

27. The compound according to Claim 1 which is:



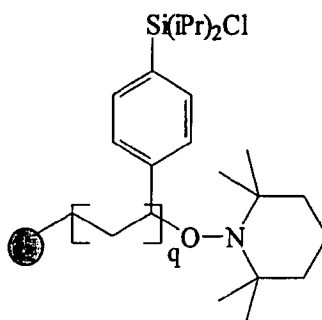
wherein  is a poly(styrene-divinyl benzene) resin with 1% to 2% divinyl benzene content, q is from 1 to 100 with an average between 10 and 60, and the isocyanate content is 1 to 6 mMol per gram.

28. The compound according to Claim 1 which is:



wherein is a poly(styrene-divinyl benzene) resin with 1% to 2% divinyl benzene content, q is from 1 to 100 with an average between 10 and 60, and the silicon content is 1 to 6 mMol per gram.

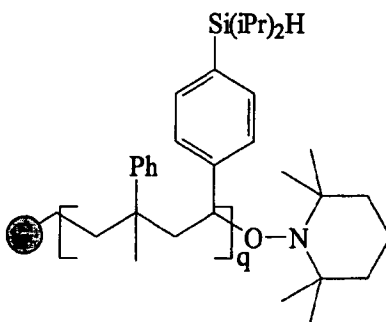
- 5 29. The compound according to Claim 1 which is:



wherein is a poly(styrene-divinyl benzene) resin with 1% to 2% divinyl benzene content, q is from 1 to 100 with an average between 10 and 60, and the silicon content is 1 to 6 mMol per gram.

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30. The compound according to Claim 1 which is:

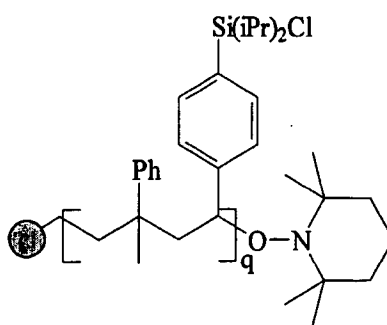



wherein is a poly(styrene-divinyl benzene) resin with 1% to 2% divinyl benzene content, q is from 1 to 50 with an average between 5 and 30 and the silicon content is 0.5 to 3 mMol/gm.

15

31. The compound according to Claim 1 which is:

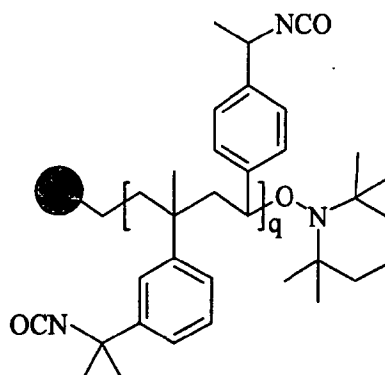
-60-



wherein  is a poly(styrene-divinyl benzene) resin with 1% to 2% divinyl benzene content, q is from 1 to 50 with an average between 5 and 30 and the silicon content is 0.5 to 3 mMol/gm.

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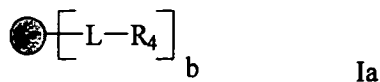
32. The compound according to Claim 1 which is



wherein \bullet is a poly(styrene-divinylbenzene) resin with 1% to 2% divinylbenzene content, q is from 1 to 50 with an average of between 5 and 30, and the isocyanate content is 1 to 6 mMol per gram.

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33. A process for the preparation of a compound of Formula Ia



wherein

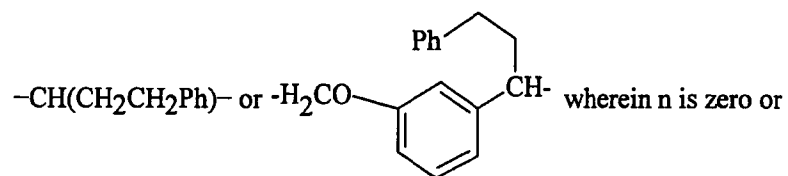
● is an insoluble solid support selected from the group consisting of poly(styrene-divinylbenzene), macroreticular poly(styrene-divinylbenzene), polystyrene which is radiation grafted to

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- polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene) and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) wherein the insoluble solid support is in a shape selected from a bead, a tube, a rod, a ring, a disk or a well;

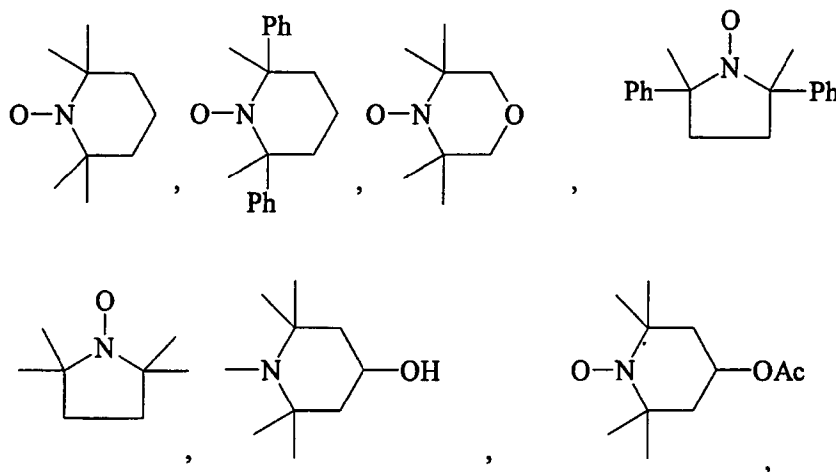
L is $-\text{CH}_2-$, $-\text{C}(\text{CH}_3)_2-$, $-\text{CH}(\text{CH}_3)-$, $-(\text{CH}_2)_n\text{CH}(\text{CN})-$,
 $-(\text{CH}_2)_n\text{CH}(\text{CO}_2\text{Me})-$, $-(\text{CH}_2)_n\text{CH}(\text{Ph})-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3, \text{Ph})-$,



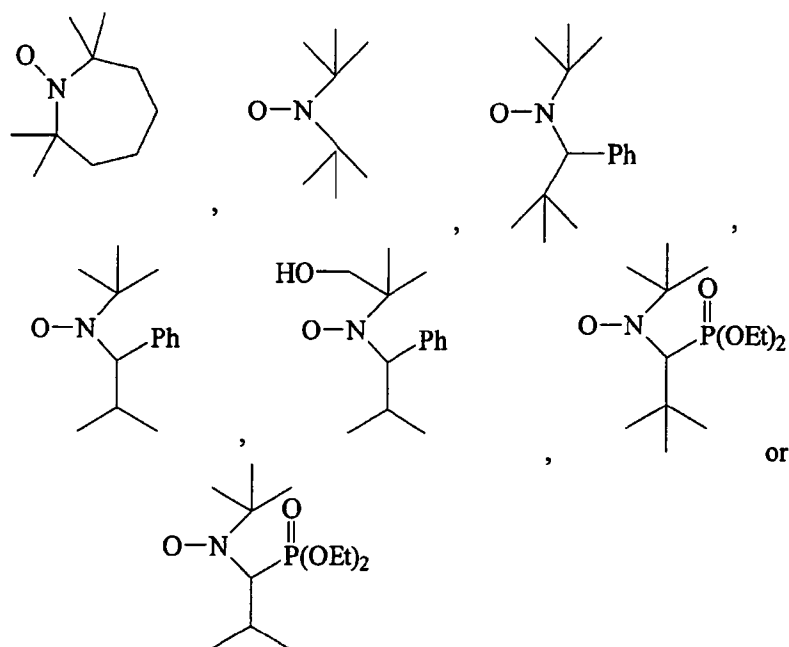
an integer from 1 to 5;

- b is mMol content of solid-supported initiator per gram of insoluble solid support and is about 0.1 to 5.0 mMol per gram;

R⁴ is



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which comprises the steps of: Step 1) chemical modification of an insoluble solid support as defined above to covalently attach multiple nitroxide substituents to the insoluble solid support via a benzylic carbon-oxygen bond forming reaction; and Step 2) washing the nitroxide-modified insoluble solid support with one or more solvents to remove excess reagents and by-products to afford a compound of Formula Ia.

34. The process according to Claim 33 wherein the nitroxide in Step 1) is TEMPO.

35. The process according to Claim 33 where the solvent in Step 2 is N,N-dimethylformamide, dichloromethane, methanol, water, or hexane.

36. The process according to Claim 33 which comprises the steps of: Step 1) dissolution of a base addition salt of a nitroxide in one or more solvents; Step 2) addition of the previous solution to an insoluble solid support containing benzylic chloro or bromo groups; Step 3) shaking or stirring at about 0°C to about 40°C for about 12 to about 48 hours under an inert atmosphere; and Step 4) washing the nitroxide-modified insoluble solid support with one or

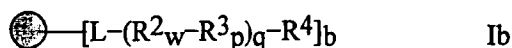
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more solvents to remove the excess unreacted reagents and by-products to afford a compound of Formula Ia.


37. The process according to Claim 36 wherein the base addition salt of a nitroxide is the sodium, potassium, lithium, or tetrabutylammonium salt of TEMPO.

38. The process according to Claim 36 wherein the solvent in Step 4) is N,N-dimethylformamide, dichloromethane, methanol, water, or hexane.

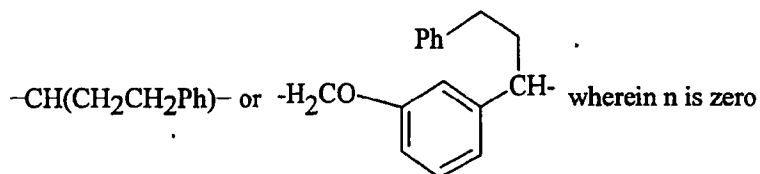
39. A process for preparing a compound of Formula Ib:



wherein:

 is an insoluble solid support selected from the group consisting of poly(styrene-divinylbenzene), macroreticular poly(styrene-divinylbenzene), polystyrene which is radiation grafted to polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene) and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) wherein the insoluble solid support is in a shape selected from a bead, a tube, a rod, a ring, a disk, or a well;

L is $-\text{CH}_2-$, $-\text{C}(\text{CH}_3)_2-$, $-\text{CH}(\text{CH}_3)-$, $-(\text{CH}_2)_n\text{CH}(\text{CN})$,
 $-(\text{CH}_2)_n\text{CH}(\text{CO}_2\text{Me})-$, $-(\text{CH}_2)_n\text{CH}(\text{Ph})-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3, \text{Ph})-$,



or an integer from 1 to 5;

w is zero or an integer from 1 to 10;

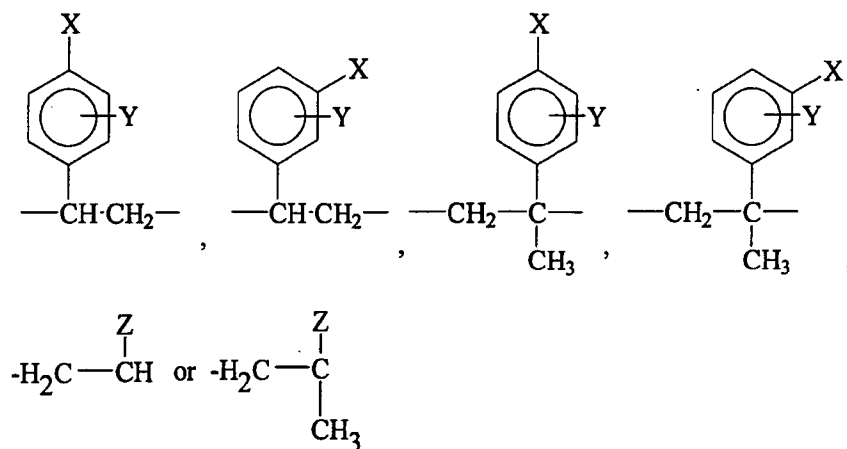
p is zero or an integer from 1 to 10;

q is zero or an integer from 1 to 300;

b is mMol content of solid-supported initiator or polymer per gram of insoluble solid support and is about 0.1 to 5.0 mMol per gram;

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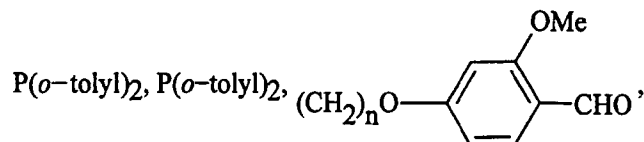
R^2 and R^3 are each independently the same or different and are:



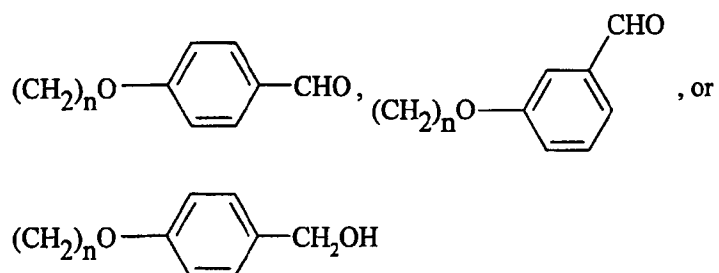
wherein

- 5 X is H, F, $(\text{CH}_2)_n\text{Cl}$, $(\text{CH}_2)_n\text{Br}$, $(\text{CH}_2)_n\text{I}$, $\text{B}(\text{OH})_2$, $(\text{CH}_2)_n\text{CH}=\text{CH}_2$, NCO , CH_2NCO , $\text{CH}(\text{CH}_3)\text{NCO}$, $\text{C}(\text{CH}_3)_2\text{NCO}$, CO_2Me , CO_2Et , $\text{CO}_2(t\text{-Bu})$, CO_2H , COCl , $\text{CO}_2\text{CH}(\text{CF}_3)_2$, CO_2Ph , $\text{CO}_2(\text{pentafluorophenyl})$, $\text{CO}_2(\text{pentachlorophenyl})$, $\text{CO}_2(\text{N-succinimidyl})$, $\text{C}(\text{OMe})_3$, $\text{C}(\text{OEt})_3$, $(\text{CH}_2)_n\text{OH}$, $(\text{CH}_2)_n\text{CH}(\text{OH})\text{CH}_2\text{OH}$, $(\text{CH}_2)_n\text{SH}$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{SH}$, $\text{CH}_2)_n\text{NHC}(=\text{S})\text{NH}_2$, $(\text{CH}_2)_n\text{NH}_2$, $(\text{CH}_2)_n\text{N}(\text{Me})_2$, $(\text{CH}_2)_n\text{N}(\text{Et})_2$, $(\text{CH}_2)_n(\text{iPr})_2$, $\text{CH}(\text{CH}_3)\text{NH}_2$, $\text{C}(\text{CH}_3)_2\text{NH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NHCH}_2\text{CH}_2\text{NH}_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$, $\text{CH}_2\text{NHCH}_2\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{NH}_2)_2$, $\text{CH}_2\text{N}(\text{CH}_2\text{CH}_2\text{OH})_2$, $(\text{CH}_2)_n(\text{morpholin-4-yl})$, $(\text{CH}_2)_n(\text{piperidin-1-yl})$, $(\text{CH}_2)_n(4\text{-methypiperazin-1-yl})$, $\text{N}(\text{SO}_2\text{CF}_3)_2$, $(\text{CH}_2)_n\text{CHO}$, $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{iPr})_2\text{H}$, $(\text{CH}_2)_n\text{Si}(\text{Me})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Et})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(i\text{-Pr})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(t\text{Bu})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Ph})_2\text{Cl}$, $(\text{CH}_2)_n\text{Si}(\text{Ph})(t\text{Bu})\text{Cl}$, $\text{P}(\text{Ph})_2$,

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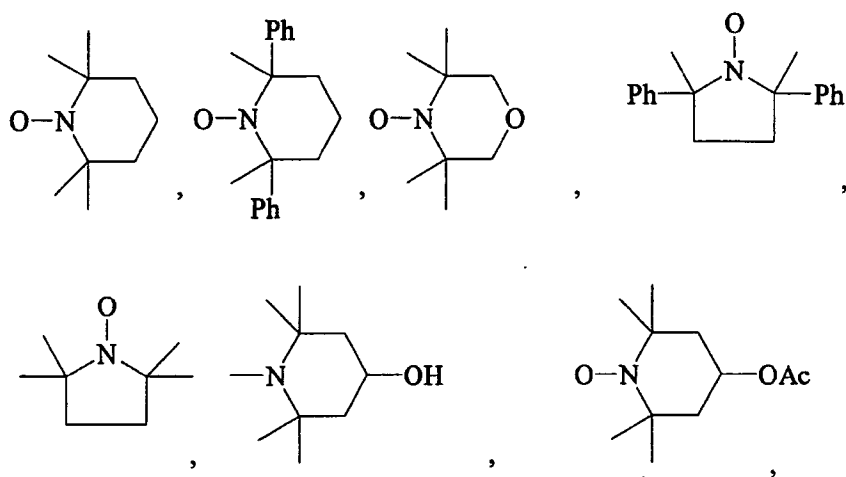
wherein n is zero or an integer from 1 to 5;

Y is H, Cl, Br, F, OH or OMe;

5

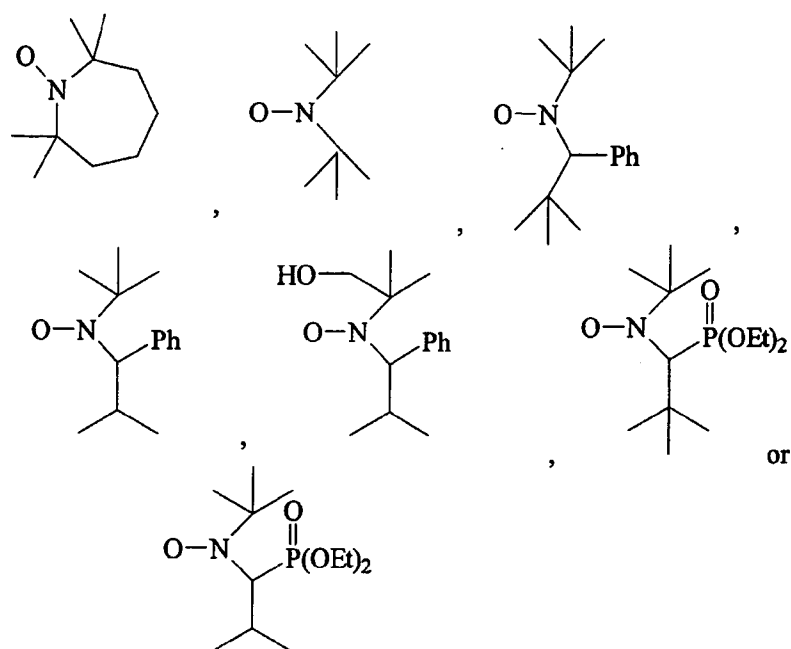
Z is NCO, CO₂Me, CO₂Et, CO₂(*i*-Pr), CO₂(*n*-Bu), CO₂(*t*-Bu), CN, CO₂H, COCl, CO₂CH(CF₃)₂, CO₂(pentafluorophenyl), CO₂(pentachlorophenyl), CO₂Ph, CO₂(N-succinimidyl), C(OMe)₃, C(OEt)₃, CON(OCH₃)CH₃, CHO, CH₂OH or C(CH₃)₂OH;

\mathbb{R}^4 is

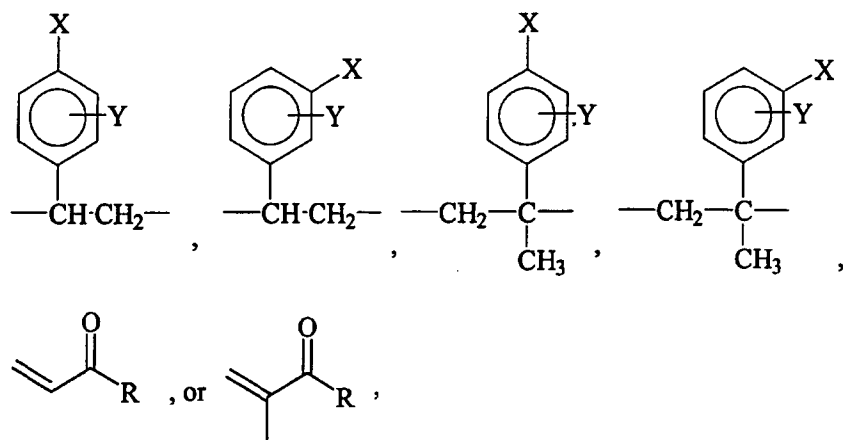


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-66-



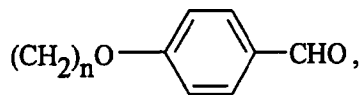
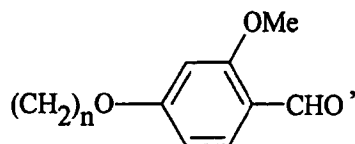
which comprises the steps of: Step 1) chemical modification of an insoluble support to covalently attach multiple cyclic nitroxide substituents to the solid support via a benzylic carbon-oxygen bond forming reaction; Step 2) washing the nitroxide-modified solid support to remove excess reagents and by-products; Step 3) heating the nitroxide-modified solid support in one or more substituted styrene or acrylate monomers selected from the group consisting of:



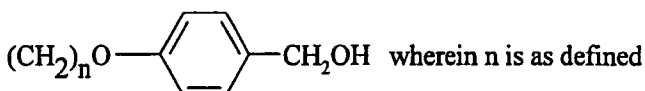
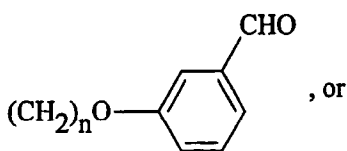
wherein

-67-

X^1 , H, F, $(CH_2)_nCl$, $(CH_2)_nBr$, $(CH_2)_nI$, $B(OH)_2$,
 $(CH_2)_nCH=CH_2$, NCO, CH_2NCO , $CH(CH_3)NCO$,
 $C(CH_3)_2NCO$, CO_2Me , CO_2Et , $CO_2(t-Bu)$, CO_2H , $COCl$,
 $CO_2CH(CF_3)_2$, CO_2Ph , CO_2 (pentafluorophenyl),
 CO_2 (pentachlorophenyl), CO_2 (N-succinimidyl), $C(OMe)_3$,
 $C(OEt)_3$, $(CH_2)_nOH$, $(CH_2)_nCH(OH)CH_2OH$, $(CH_2)_nSH$,
 $CH_2NHCH_2CH_2SH$, $(CH_2)_nNHC(=S)NH_2$, $(CH_2)_nNH_2$,
 $(CH_2)_nN(Me)_2$, $(CH_2)_nN(Et)_2$, $(CH_2)_n(iPr)_2$,
 $CH(CH_3)NH_2$, $C(CH_3)_2NH_2$, $CH_2NHCH_2CH_2NH_2$,
 $CH_2NHCH_2CH_2NHCH_2CH_2NH_2$, $CH_2N(CH_2CH_2NH_2)_2$,
 $CH_2NHCH_2CH_2N(CH_2CH_2NH_2)_2$,
 $(CH_2)_nNHCO_2CH_2CH_2Si(CH_3)_3$,
 $CH(CH_3)NHCO_2CH_2CH_2Si(CH_3)_3$,
 $C(CH_3)_2NHCO_2CH_2CH_2Si(CH_3)_3$, $CH_2N(CH_2CH_2OH)_2$,
 $(CH_2)_n$ (morpholin-4-yl), $(CH_2)_n$ (piperidin-1-yl),
 $(CH_2)_n$ (4-methylpiperazin-1-yl), $N(SO_2CF_3)_2$,
 $(CH_2)_nCHO$, $(CH_2)_nSi(Me)_2H$, $(CH_2)_nSi(Et)_2H$,
 $(CH_2)_nSi(iPr)_2H$, $(CH_2)_nSi(Me)_2Cl$, $(CH_2)_nSi(Et)_2Cl$,
 $(CH_2)_nSi(i-Pr)_2Cl$, $(CH_2)_nSi(tBu)_2Cl$, $(CH_2)_nSi(Ph)_2Cl$,
 $(CH_2)_nSi(Ph)(tBu)Cl$, $P(Ph)_2$, $P(o-tolyl)_2$,



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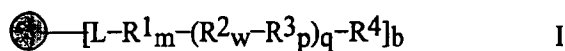


above;


Y is as defined above;

- 5 R is CO₂Me, CO₂Et, CO₂(*i*-Pr), CO₂(*n*-Bu), CO₂(*t*-Bu), CN, CO₂H, COCl, CO₂CH(CF₃)₂, CO₂(pentafluorophenyl), CO₂(pentachlorophenyl), CO₂Ph, CO₂(N-succinimidyl), CON(OCH₃)CH₃, or CHO under an inert atmosphere to about 120°C to about 150°C for about 4 to about 48 hours to
- 10 grow polymeric chains onto the solid support; Step 4) rinsing the solid-supported polymer with one or more solvents to remove excess monomers and soluble polymer; and Step 5) functional group deprotection and transformation of R and X as necessary to afford a compound of Formula Ib.

- 15 40. The process according to Claim 39 wherein the cyclic nitroxide substituent in Step 1) is TEMPO.
41. The process according to Claim 39 wherein the solvent in Step 4 is N,N-dimethylformamide, dichloromethane, methanol, water, or hexane.
- 20 42. A process for preparing a compound of Formula I



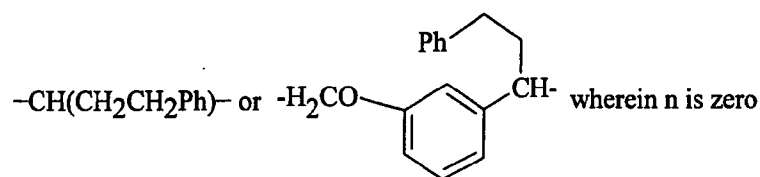
wherein

25  is an insoluble solid support selected from the group consisting of poly(styrene-divinylbenzene), macroreticular poly(styrene-

-69-

divinylbenzene), polystyrene which is radiation grafted to polypropylene, polystyrene which is radiation grafted to polyethylene, polystyrene which is radiation grafted to poly(tetrafluoroethylene) and polystyrene which is radiation grafted to poly(ethylene-tetrafluoroethylene) wherein the insoluble solid support is in a shape selected from a bead, a tube, a rod, a ring, a disk, or a well;

L is $-\text{CH}_2-$, $-\text{C}(\text{CH}_3)_2-$, $-\text{CH}(\text{CH}_3)-$, $-(\text{CH}_2)_n\text{CH}(\text{CN})-$, $-(\text{CH}_2)_n\text{CH}(\text{CO}_2\text{Me})-$, $-(\text{CH}_2)_n\text{CH}(\text{Ph})-$, $-(\text{CH}_2)_n\text{C}(\text{CH}_3, \text{Ph})-$,



or an integer from 1 to 5;

m is zero or an integer from 1 to 100;

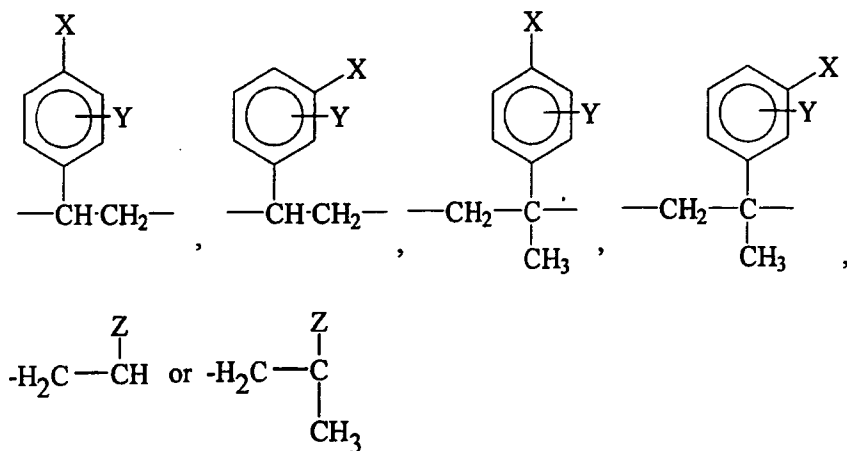
w is zero or an integer from 1 to 10;

p is zero or an integer from 1 to 10;

q is zero or an integer from 1 to 300;

b is mMol content of solid-supported initiator or polymer per gram of insoluble solid support and is about 0.1 to 5.0 mMol per gram;

R^1 , R^2 and R^3 are each independently the same or different and are



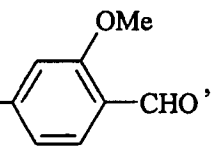
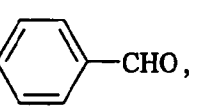
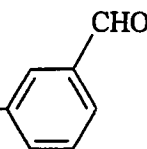
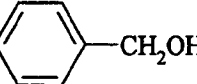
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wherein

X is H, F, $(\text{CH}_2)_n\text{Cl}$, $(\text{CH}_2)_n\text{Br}$, $(\text{CH}_2)_n\text{I}$, $\text{B}(\text{OH})_2$, $(\text{CH}_2)_n\text{CH}=\text{CH}_2$, NCO , CH_2NCO , $\text{CH}(\text{CH}_3)\text{NCO}$, $\text{C}(\text{CH}_3)_2\text{NCO}$, CO_2Me , CO_2Et , $\text{CO}_2(t-$

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Bu), CO₂H, COCl, CO₂CH(CF₃)₂, CO₂Ph,
 CO₂(pentafluorophenyl), CO₂(pentachlorophenyl), CO₂(N-
 succinimidyl), C(OMe)₃, C(OEt)₃, (CH₂)_nOH,
 (CH₂)_nCH(OH)CH₂OH, (CH₂)_nSH, CH₂NHCH₂CH₂SH,
 5 (CH₂)_nNHC(=S)NH₂, (CH₂)_nNH₂, (CH₂)_nN(Me)₂, (CH₂)_nN(Et)₂,
 (CH₂)_n(iPr)₂, CH(CH₃)NH₂, C(CH₃)₂NH₂, CH₂NHCH₂CH₂NH₂,
 CH₂NHCH₂CH₂NHCH₂CH₂NH₂, CH₂N(CH₂CH₂NH₂)₂,
 CH₂NHCH₂CH₂N(CH₂CH₂NH₂)₂, CH₂N(CH₂CH₂OH)₂,
 (CH₂)_n(morpholin-4-yl), (CH₂)_n(piperidin-1-yl), (CH₂)_n(4-
 10 methypiperazin-1-yl), N(SO₂CF₃)₂, (CH₂)_nCHO, (CH₂)_nSi(Me)₂H,
 (CH₂)_nSi(Me)₂H, (CH₂)_nSi(Et)₂H, (CH₂)_nSi(iPr)₂H,
 (CH₂)_nSi(Me)₂Cl, (CH₂)_nSi(Et)₂Cl, (CH₂)_nSi(*i*-Pr)₂Cl,
 (CH₂)_nSi(*t*Bu)₂Cl, (CH₂)_nSi(Ph)₂Cl, (CH₂)_nSi(Ph)(*t*Bu)Cl, P(Ph)₂,

P(*o*-tolyl)₂, P(*o*-tolyl)₂, (CH₂)_nO-,
 15 (CH₂)_nO-, (CH₂)_nO-, or
 (CH₂)_nO- where n is zero or an integer

from 1 to 5;

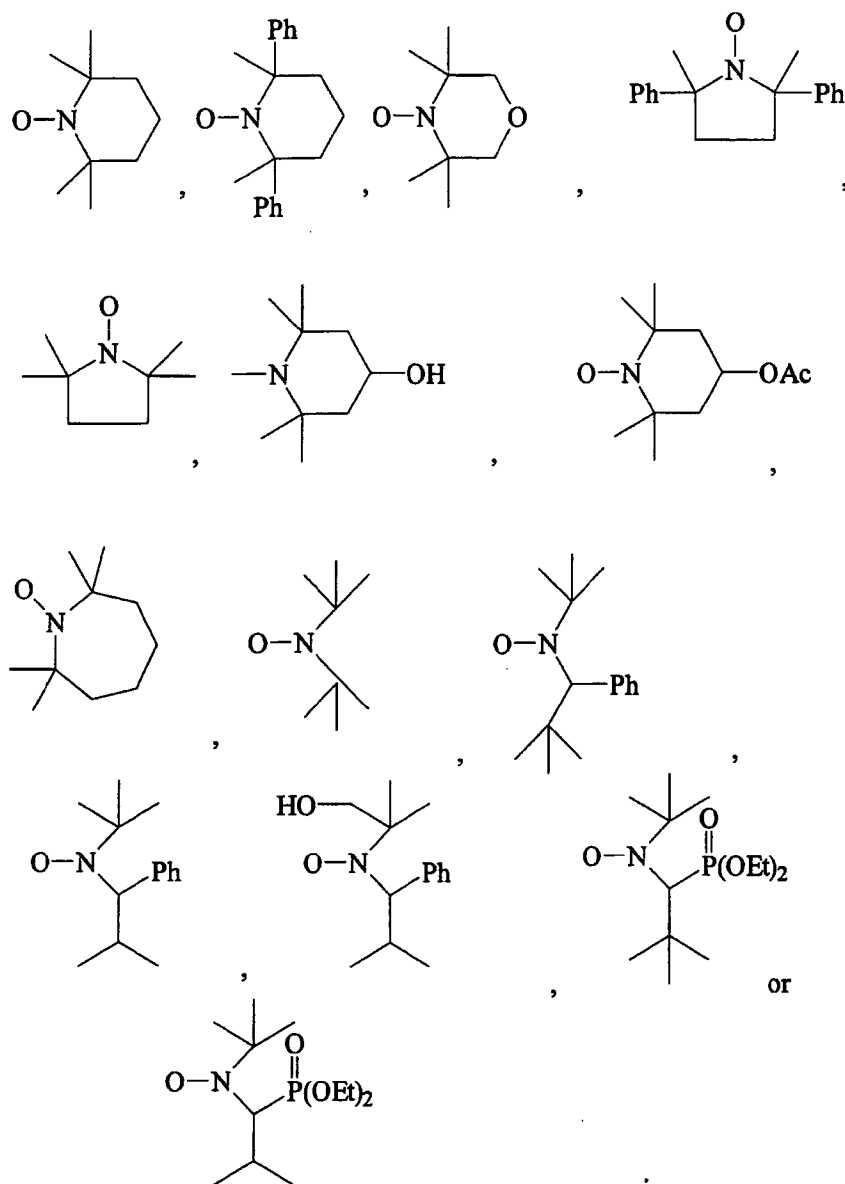
Y is H, Cl, Br, F, OH or OMe;

Z is NCO, CO₂Me, CO₂Et, CO₂(*i*-Pr), CO₂(*n*-Bu), CO₂(*t*-Bu), CN,

20 CO₂H, COCl, CO₂CH(CF₃)₂, CO₂(pentafluorophenyl),
 CO₂(pentachlorophenyl), CO₂Ph, CO₂(N-succinimidyl), C(OMe)₃,
 C(OEt)₃, CON(OCH₃)CH₃, CHO, CH₂OH or C(CH₃)₂OH;

R⁴ is

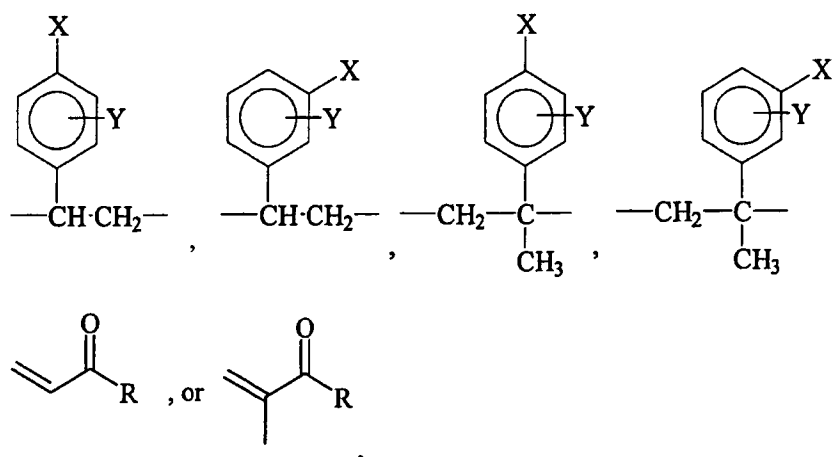
-71-



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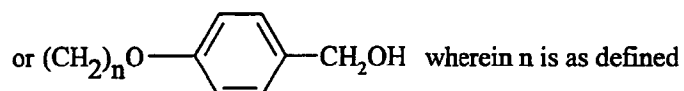
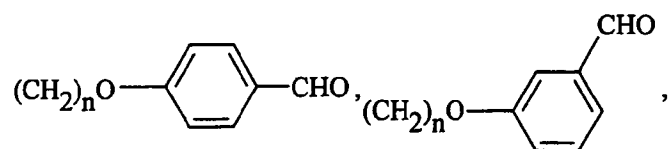
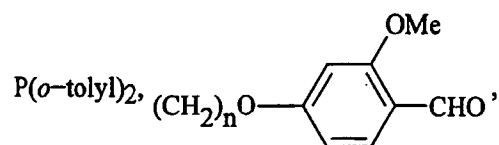
which comprises the steps of : Step 1) chemical modification of an insoluble support to covalently attach multiple cyclic nitroxide substituents to the solid support via a benzylic carbon-oxygen bond forming reaction; Step 2) washing the nitroxide-modified solid support to remove excess reagents and by-products; Step 3) heating the nitroxide-modified solid support in one or more substituted styrene or acrylate monomers selected from the group consisting of:

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wherein X^1 is H, F, $(CH_2)_nCl$, $(CH_2)_nBr$, $(CH_2)_nI$, $B(OH)_2$,
 $(CH_2)_nCH=CH_2$, NCO, CH_2NCO , $CH(CH_3)NCO$,
 5 $C(CH_3)_2NCO$, CO_2Me , CO_2Et , $CO_2(t-Bu)$, CO_2H , $COCl$,
 $CO_2CH(CF_3)_2$, CO_2Ph , $CO_2(\text{pentafluorophenyl})$,
 $CO_2(\text{pentachlorophenyl})$, $CO_2(N\text{-succinimidy})$, $C(OMe)_3$,
 $C(OEt)_3$, $(CH_2)_nOH$, $(CH_2)_nCH(OH)CH_2OH$, $(CH_2)_nSH$,
 $CH_2NHCH_2CH_2SH$, $(CH_2)_nNHC(=S)NH_2$, $(CH_2)_nNH_2$,
 10 $(CH_2)_nN(Me)_2$, $(CH_2)_nN(Et)_2$, $(CH_2)_n(iPr)_2$,
 $CH(CH_3)NH_2$, $C(CH_3)_2NH_2$, $CH_2NHCH_2CH_2NH_2$,
 $CH_2NHCH_2CH_2NHCH_2CH_2NH_2$, $CH_2N(CH_2CH_2NH_2)_2$,
 $CH_2NHCH_2CH_2N(CH_2CH_2NH_2)_2$,
 $(CH_2)_nNHCO_2CH_2CH_2Si(CH_3)_3$,
 15 $CH(CH_3)NHCO_2CH_2CH_2Si(CH_3)_3$,
 $C(CH_3)_2NHCO_2CH_2CH_2Si(CH_3)_3$, $CH_2N(CH_2CH_2OH)_2$,
 $(CH_2)_n(\text{morpholin-4-yl})$, $(CH_2)_n(\text{piperidin-1-yl})$,
 $(CH_2)_n(4\text{-methypiperazin-1-yl})$, $N(SO_2CF_3)_2$,
 $(CH_2)_nCHO$, $(CH_2)_nSi(Me)_2H$, $(CH_2)_nSi(Et)_2H$,
 20 $(CH_2)_nSi(iPr)_2H$, $(CH_2)_nSi(Me)_2Cl$, $(CH_2)_nSi(Et)_2Cl$,
 $(CH_2)_nSi(i-Pr)_2Cl$, $(CH_2)_nSi(tBu)_2Cl$, $(CH_2)_nSi(Ph)_2Cl$,
 $(CH_2)_nSi(Ph)(tBu)Cl$, $P(Ph)_2$, $P(o\text{-tolyl})_2$,

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above;

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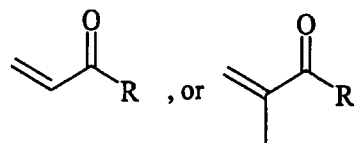
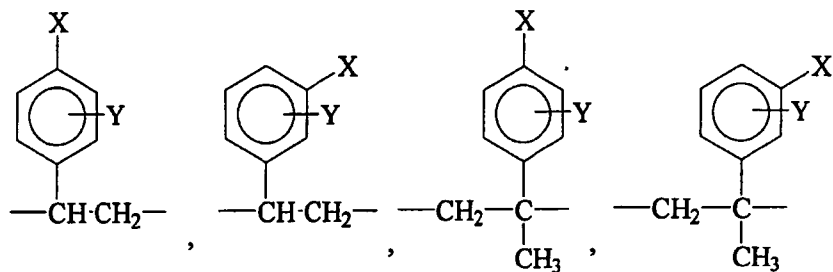
Y is as defined above;

R is CO_2Me , CO_2Et , $\text{CO}_2(i\text{-Pr})$, $\text{CO}_2(n\text{-Bu})$, $\text{CO}_2(t\text{-Bu})$, CN, CO_2H , COCl , $\text{CO}_2\text{CH}(\text{CF}_3)_2$, $\text{CO}_2(\text{pentafluorophenyl})$, $\text{CO}_2(\text{pentachlorophenyl})$, CO_2Ph , $\text{CO}_2(\text{N-succinimidyl})$, $\text{CON}(\text{OCH}_3)\text{CH}_3$, or CHO under an inert atmosphere, to about 120°

10

C to about 150°C for about 4 to about 48 hours to grow polymeric chains onto the solid support; Step 4) rinsing the solid-supported polymer with one or more solvents to remove excess monomers and soluble polymer; Step 5) heating the resulting solid-supported polymer which contains cyclic nitroxide substituents with one or more substituted styrene or acrylate monomers selected from the group consisting of:

15



wherein X^1 , Y, R and n are as defined above under an inert atmosphere, to about 120°C to about 150°C for about 4 to about 48 hours to extend the solid supported polymer; Step 6) rinsing of the solid-supported polymer with one or more solvents to remove excess monomers and soluble polymer; and Step 7) functional group deprotection and transformation of R and X as necessary to afford a compound of Formula I.

- 5
43. The process according to Claim 42 wherein the cyclic nitroxide in Step 1) in TEMPO.
- 10
44. The process according to Claim 42 wherein the solvent in Steps 4) and 6) is N,N-dimethylformamide, dichloromethane, methanol, water, or hexane.
45. The use of a compound according to Claim 42 as an solid-supported initiator for free radical polymerization.
- 15
46. The use of a compound according to Claim 42 as a solid-supported scavenger.
47. The use of a compound according to Claim 42 as a solid-supported reagent.
48. The use of a compound according to Claim 42 as a solid support in solid phase synthesis.
- 20
49. The use of a compound according to Claim 42 to facilitate purification in the practice of organic synthesis.
50. The use of a compound according to Claim 42 to facilitate purification in the practice of combinatorial chemistry.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/17038

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D295/22 C07C291/04 C08F8/30 C08F4/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D C07C C08F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DE 197 01 665 A (HANS-KNOELL-INSTITUT FUER NATURSTOFF-FORSCHUNG E.V., GERMANY;FRIEDRICH) 23 July 1998 (1998-07-23) examples 14-18	1
X,P	J.C.HODGES ET AL: "Preparation of designer resins via living free radical polymerization of functional monomers on solid support" JOURNAL OF COMBINATORIAL CHEMISTRY., vol. 2, no. 1, 2000 - 1980, pages 80-88, XP002149955 AMERICAN CHEMICAL SOCIETY, WASHINGTON., US ISSN: 1520-4766 the whole document	1



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

25 October 2000

Date of mailing of the international search report

08/11/2000

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Pauwels, G

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/17038

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	D.J. GRAVERT ET AL.: "Soluble supports tailored for organic synthesis: Parallel polymer synthesis via sequential normal/living free radical processes" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 120, 1998, pages 9481-9495, XP002149956 DC US page 9483 ----	1-42
A	BENOIT D ET AL: "Development of a Universal Alkoxyamine for Living Free Radical Polymerizations" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY,US,AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, vol. 121, no. 16, 28 April 1999 (1999-04-28), pages 3904-3920, XP002115863 ISSN: 0002-7863 cited in the application the whole document -----	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 00/17038

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19701665 A	23-07-1998	NONE	